CLINICAL STUDY OF INCIDENCE OF MALIGNANCY IN SOLITARY NODULE OF THYROID

A Dissertation Submitted to the

Dr.MGR .Medical University, Chennai

Tamilnadu

In Partial Fulfillment of the Requirements for the Degree of

M. S. (GENERAL SURGERY)

DEPARTMENT OF GENERAL SURGERY

TIRUNELVELI MEDICAL COLLEGE HOSPITAL

TIRUNELVELI

APRIL 2016

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Lastly, I express my thanks to my patients without whom this study would not have been possible.

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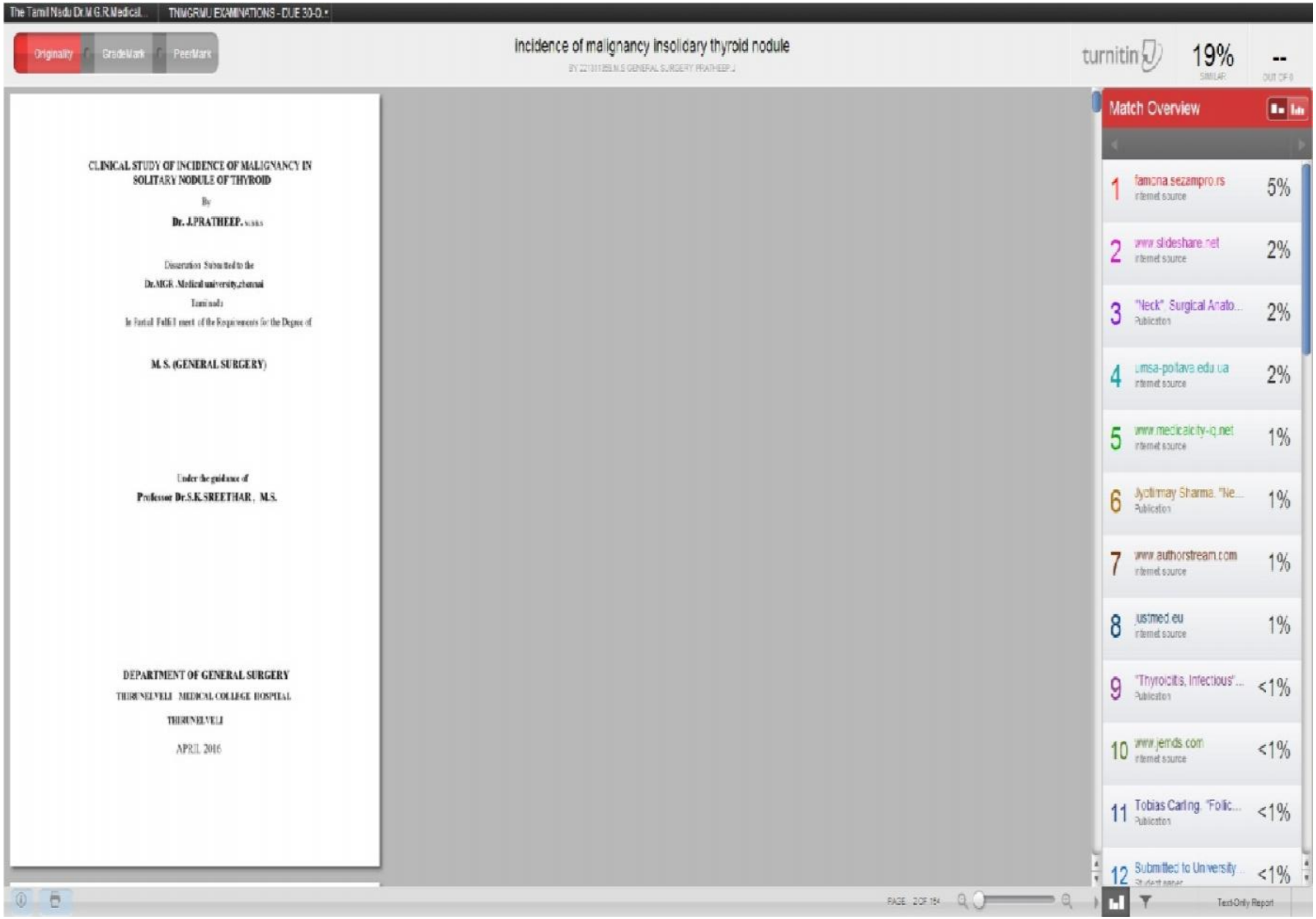
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DESIGNATION OF PRINCIPAL INVESTIGATOR: Post Graduate in MS General Surgery
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THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1. TIREC Application Form ☐
2. Study Protocol ☐
3. Department Research Committee Approval ☐
4. Patient Information Document and Consent Form in English and Vernacular Language ☐
5. Investigator's Brochure ☐
6. Proposed Methods for Patient Accrual Proposed ☐
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THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
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LIST OF ABBREVATIONS

AG	Adenomatous goiter
ATC	Anaplastic thyroid carcinoma
ECG	Electrocardiogram
FNAC	Fine needle aspiration cytology
HPE	Histopathological examination
MIT	Monoiodotyrosine
MNG	Multinodular goiter
MTC	Medullary thyroid carcinoma
RLN	Recurrent laryngeal nerve
SNT	Solitary nodule thyroid
T3	Tri-iodotyrosine
T4	Thyroxine
TBG	Thyroxine binding globulin
TR	Thyroid hormone receptor
USG	Ultrasonography

ABSTRACT

Background

Solitary nodule of thyroid has increased in incidence in the present day as compared to two decades before. Because of possibility of malignancy, some clinicians especially those in surgical subspecialities recommended that all nodules have to be removed.

Objectives of the Study

1. To determine the incidence of malignancy in solitary nodule of thyroid in general population and in relation to age and sex.
2. To determine the incidence of solitary nodule of thyroid turning out to be multi-nodular goiter. To study the incidences of euthyroid, hyperthyroid or hypothyroid states in patients presenting with solitary nodule of thyroid.
3. To study the role of FNAC in the management of solitary nodule of thyroid.
4. To determine the incidence of adenoma, carcinoma and thyroiditis as a cause of solitary nodule of thyroid in T.V.M.C, Thirunelveli.

MATERIALS AND METHODS

Source of Data

Patients with Solitary nodule thyroid admitted to various surgical wards in T.V.M.C, Thirunelveli during the period of September 2014 — August 2015.

Method of Collecting Data

Data collection by meticulous history taking and clinical examination, appropriate laboratory and radiological investigations, operative findings, histopathological report and follow up of cases.

The study of minimum 50 cases selected by Random Sampling Technique admitted tc surgical wards of T.V.M.C, Thirunelveli during the period of September 2014 -August 2015.

Inclusion Criteria

Patients admitted to surgical wards of T.V.M.C, Thirunelveli with features of SNT.

Exclusion Criteria

- Patients with diffuse enlargement of thyroid.
- Patients presenting with MNG clinically*.
- Patients refusing for investigations / management.

Results:

Commonest presentation of solitary thyroid nodule was asymptomatic. The Peak incidence of solitary nodule was observed in 3^{rd} to 5^{th} decade, constituting 60% of the cases studied. Females predominated in number over males in occurrence of solitary nodule in ratio of 1:11.5. 36% of all clinically solitary nodule turned out to be multi-nodular goiter. The common causes of solitary nodule was MNG (36%), follicular adenoma (22%), adenomatous goiter (24%). 94% 0f cases presented with euthyroid state. Incidence of malignancy in solitary thyroid nodule was 12%. Male to female ratio in case of malignant nodule was1:5. Incidence of carcinoma in males presenting as solitary nodule was higher (25%) compared to that of females (10.87%). The most common cause of malignancy was papillary carcinoma (67%) followed by follicular carcinoma (33%). .

Interpretation and Conclusion:

Solitary nodule of thyroid is more common in 3rd to 5th decades. Solitary nodule of thyroid are more common in females. Most of the patients presenting with solitary nodule of thyroid are euthyroid and only a small percentage of patient with toxicity or hypothyroidism USG can be accurately used to detect patients with multinodulary goiter who clinically present as solitary nodule of thyroid. Common causes of solitary nodule of thyroid are MNG, follicular adenoma and adenomatous goiter. Incidence of malignancy in male patients presenting with solitary nodule of thyroid is more when compared to female. The most common cause of malignancy in solitary nodule is papillary carcinoma followed by follicular carcinoma.

Key words : solitary nodule, malignancy, euthyroid.

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INTRODUCTION

The solitary thyroid nodule has aroused interest of thyroidologist since the time of Warren H Cole (1949) and his study concluded that incidence of malignancy is higher when compared with multinodular goitre.

Thyroid nodules are very common entities, though varying in incidence in different geographical regions. the prevalence of palpable nodules in general population is 4-7%. Solitary nodules of thyroid are about four times more common in women than in men. Overall incidence of malignancy in solitary thyroid nodule ranges from 10-30%.

Definition:

A single nodule in the thyroid is a definite clinical entity with important pathological significance. It is necessary to consider the status of opposite lobe when considering the 'solitariness' of the nodule. Ignoring palpability of opposite lobe is likely to lead to a higher incidence of solitary nodule turning out to be multi-nodular goiter.

Another factor that influences the ultimate histopathological outcome of solitary nodule of solitary nodule thyroid is whether the definition of solitariness is entirely clinical or proved by investigations like U/S, radio iodine scan etc. in general a solitary nodule is defined as "a palpable single clinically detected nodule in the thyroid gland that is otherwise normal." Visibility or palpability of opposite thyroid lobe precludes inclusion of such cases in this group.

The usual presentation of a thyroid nodule is an asymptomatic mass that is discovered by either the patient or the clinician. Nodules of at least 0.5cm to 1cm can be usually be detected by palpation, although estimates of nodule size varies from physician to physician. It can be difficult to palpate any nodule in patient with a thick, short neck .

The thyroid nodule has been subject of vigorous controversy with divergent opinions expressed by those who had wide experience in this field. The optimal management of thyroid nodule continues to be a source of controversy and the operative intervention recommended by most of surgeons is not always considered divine by some physicians advocating either observation or suppression .

The importance of discrete swelling lies in the risk of neoplasia compared with other thyroid swellings. Some 15% of isolated swelling prove to be malignant and non-neoplastic, largely consisting of malignancy or follicular adenoma in clinically dominant swelling is approximately half that of truly isolated swelling ,it is substantial and cannot be ignored .

Because of possibility of malignancy, some clinicians especially those in surgical subspecialties recommend that all nodules have to be removed. On the other hand endocrinologist recommends FNAC performed as initial step of evaluation in order to avoid unnecessary surgery.

AIMS AND OBJECTIVES

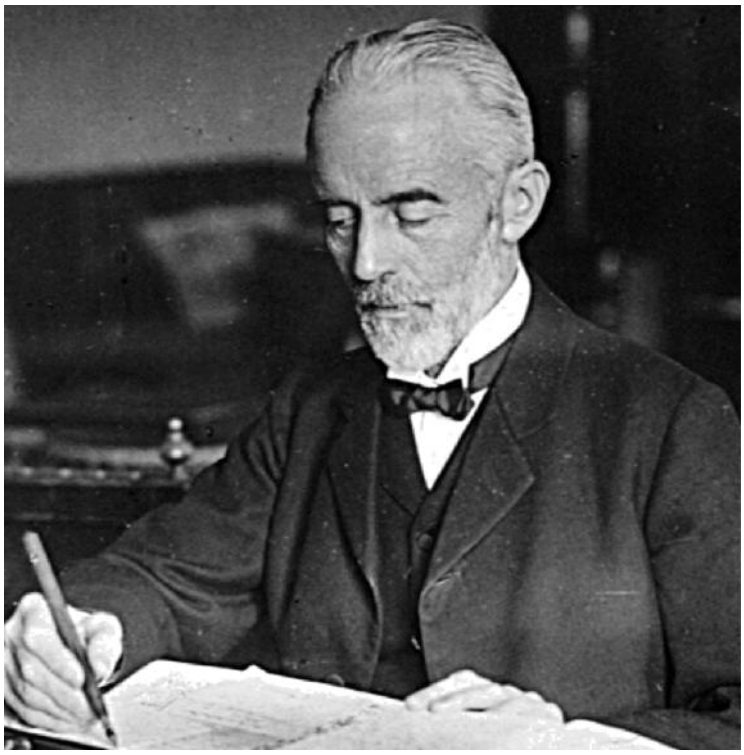
1. To determine the incidence of solitary nodule thyroid in relation to age and sex
2. To determine the incidence of solitary nodule of thyroid turning out to be malignancy
3. To determine the incidence of solitary nodule of thyroid turning out to be multi nodular goiter
4. To study the incidences of euthyroid, hyperthyroid or hypothyroid states in patients presenting with solitary nodule of thyroid.
5. To study the role of FNAC in the management of solitary nodule of thyroid.
6. To determine the incidence of adenoma, carcinoma and thyroiditis as a cause of solitary nodule of thyroid in Thirunelveli medical college .

REVIEW OF LITERATURE

Historical review

Goiters (from the Latin *guttur*, throat), defined as an enlargement of the thyroid, have been recognized since 2700 B.C. The term *thyroid gland* (Greek *thyreoeides*, shield-shaped) is, however, attributed to Thomas Wharton. In 1776, the thyroid was classified as a ductless gland by Albrechtvon Haller and was thought to have numerous functions ranging from lubrication of the larynx to acting as a reservoir for blood to provide continuous flow to the brain, to beautifying women's necks. Burnt seaweed was considered to be the most effective treatment for goiters.

The first accounts of thyroid surgery for the treatment of goiters were given by Roger Frugardi in 1170. In response to failure of medical treatment, two setons were inserted at right angles into the goiter and tightened twice daily until the goiter separated. The open wound was treated with caustic powder and left to heal. However, thyroid surgery continued to be hazardous with prohibitive mortality rates (>40%) until the latter half of the nineteenth century, when advances in general anesthesia, antisepsis, and hemostasis enabled surgeons to perform thyroid surgery with significantly reduced mortality and morbidity rates. The most notable thyroid surgeons were Emil Theodor Kocher (1841– 1917) and C.A. Theodor Billroth (1829–1894), who performed thousands of operations with increasingly successful results. However, as more patients survived thyroid operations, new problems and issues became apparent. After total thyroidectomy, patients (particularly children) became myxedematous with cretinous features. Myxedema was first effectively treated in 1891 by George Murray using a subcutaneous injection of an extract of sheep's thyroid and later, Edward Fox demonstrated that oral therapy was equally effective. In 1909, Kocher was awarded the Nobel Prize for medicine in recognition "for his works on the physiology, pathology, and surgery of the thyroid gland."



Theoder Kocher, Father of thyroid surgery

Kocher Billroth

EMBRYOLOGY

Normal Development

The thyroid gland appears by the end of the third week as an epithelial thickening of the floor of the pharynx at the level of the first pharyngeal pouch. This, the large median thyroid anlage, may be a diverticulum or a solid bud. Cranial growth of the tongue, together with elongation of the embryo, carries the origin of the thyroid gland far cranial to the gland itself. The site of this origin is the foramen cecum of the adult tongue. In some individuals it is not grossly visible.

The thyroid gland remains connected with the foramen cecum by a minute, solid thyroglossal duct that passes through, or anterior to, the hyoid bone. By the fifth week of gestation, this duct usually becomes fragmented; persistence of any portion is not unusual. In about 50 percent of the population, the duct can be traced distally to the pyramidal lobe of the thyroid gland .

The developing gland, at first an irregular plate, develops two lateral wings connected by the isthmus. Follicles appear during the second month of gestation and increase through the fourth month. Colloid formation and uptake of radioactive iodine begin at about the eleventh week.

Epithelial structures, the paired lateral anlages, are formed from the ventral portions of the fourth and fifth branchial pouches. This structure, the well-known ultimobranchial body (caudal pharyngeal pouch complex), becomes lost in the developing thyroid gland, and its cells become dispersed as the C (calcitonin) cells among the thyroid follicles.

Present evidence suggests that the primary origin of the calcitonin-producing cells of the thyroid gland is the neural crest of the embryo. From the neural crest these cells migrate to the ultimobranchial body, and later become part of the thyroid gland. C cells belong to a group of

neural-crest derivatives known as APUD (amine precursor uptake and decarboxylation) cells. Tumors of the APUD system are collectively called "apudomas." Congenital Anomalies

Lingual Thyroid

Occasionally the thyroid gland is not in the normal cervical position, but lies beneath the epithelium of the tongue, at the site of the foramen cecum.lingual thyroid results from a failure of the median anlage to descend from the pharynx. The lingual thyroid gland is usually small but normal and is the only thyroid tissue present. Radioactive iodine scintigraphy will aid in the diagnosis and will determine the presence of other thyroid tissue in the patient.

A thyroid gland may be found anywhere along the track from the foramen cecum to the normal site. Such "partially descended" glands are rare. Total excision of a lingual thyroid is necessary. It requires care, because the gland is well vascularized by the lingual arteries. In one series,2 out of 12 lingual thyroids were malignant. If no malignancy is reported from frozen sections, the excised tissue can be implanted into the anterior abdominal wall.

Persistent Remnants of the Thyroglossal Duct

The foramen cecum of the tongue and the pyramidal lobe of the thyroid gland are normal remnants of the thyroglossal duct. Thyroglossal duct cysts account for 62.8 percent of all the congenital masses of the neck.

Primary carcinoma in thyroglossal duct cyst occurs in less than 1 percent of cases. Walton and Koch presented a case of thyroglossal duct cyst with papillary carcinoma,

Medullary thyroid cancer has not been reported because there are no C cells in the pyramidal lobe (the parafollicular C cells arise from the lateral thyroid anlage).Frequently, individuals who have ectopic thyroid also have an absence of normal thyroid. Therefore, before the ectopic thyroid is excised, it is important to evaluate whether it is the only thyroid tissue in the

body. Between the foramen cecum and the pyramidal lobe is a very small epithelial tube, usually broken in several places. Occasionally these epithelial fragments hypertrophy, secrete fluid, and form cysts. Drainage or aspiration of these cysts is futile and often results in the formation of a fistula, which usually becomes infected. All fragments of the duct, foramen cecum, and midportion of the hyoid bone should be removed (Sistrunk procedure). Recurrence of the cyst is the result of failure to remove the entire duct. Failure to remove the central portion of the hyoid bone resulted in 17 percent recurrence in one series of operations.

Lateral Aberrant Thyroid

Of special interest —and a vexation to surgeon, pathologist, and patient— is lateral aberrant thyroid tissue; that is, tissue located lateral to the jugular vein. It has three morphologic manifestations.

This tissue may be found as a nodule attached by connective tissue to the mother gland. These thyroid tissue "islands," which pull away from the visceral body during development, are nevertheless normal.

The second site for lateral thyroid tissue is within lymph nodes or their remnants.

We should consider a cervical lymph node containing thyroid follicles to be clinically a metastatic thyroid carcinoma. However, the existence of heterotopic thyroid tissue within cervical glands has been reported.

The final morphologic expression of laterally aberrant thyroid tissue must be termed congenital. In a patient whose only thyroid tissue, by all appearances, was lateral aberrant thyroid tissue.

Always consider the possibility of metastatic thyroid cancer of lateral aberrant thyroid nodules.

Struma Ovari

Struma ovarii, the ovarian thyroid, is an extraordinary thyroid ectopia, although it is unrelated to the anatomic thyroid gland and is not a true congenital anomaly. Ovarian thyroid tissue is a fellow traveller with dermoid cysts and teratoma. Struma ovarii may exist in 0.2-1.3% of all ovarian tumors. Of these, 5-6% are bilateral and about 5% possess functioning thyroid tissue. Hyperthyroidism in struma ovarii may be seen in some cases. Malignancy is a possible occurrence in as many as 5% of all struma ovarii,with metastasis noted in papillary carcinoma.

ANATOMY

General Topography

The thyroid gland consists typically of two lobes, a connecting isthmus, and an ascending pyramidal lobe. One lobe, usually the right, may be smaller than the other (7 percent) or may even be completely absent (1.7 percent). The isthmus is absent in about 10 percent of thyroid glands, and the pyramidal lobe is absent in about 50 percent . A minute epithelial tube or fibrous cord, the thyroglossal duct, almost always extends between the thyroid gland and the foramen cecum of the tongue.

The thyroid gland normally extends from the level of the 5th cervical vertebra to the body of the 1st thoracic vertebra. It may lie higher (lingual thyroid), but rarely lower. The normal thyroid gland weighs about 30 g in the adult —somewhat more in females than in males. Each lobe is approximately 5 cm in length, 3 cm at its greatest width, and 2-3 cm thick. The isthmus connecting the two lobes is about 1.3 cm in breadth. The lobes have a broad lower portion and a relatively conical apex.

Capsule of the Thyroid Gland

The thyroid gland has a connective tissue capsule which is continuous with the septa, and which makes up the stroma of the organ. This is the true capsule of the thyroid.

External to the true capsule is a well developed (to a lesser or greater degree) layer of fascia derived from the pretracheal fascia. This is the false capsule, also called the perithyroid sheath or surgical capsule. Anteriorly and laterally this fascia is well developed; posteriorly it is thin and loose, permitting enlargement of the thyroid gland posteriorly. There is a thickening of the fascia that fixes the back of each lobe to the cricoid cartilage. Such thickenings are the ligaments of Berry. The false capsule, or fascia, is not removed with the gland during thyroidectomy.

The superior parathyroid glands normally lie between the true capsule of the thyroid and the fascial false capsule. The inferior parathyroids may be between the true and false capsules, within the thyroid parenchyma, or lying on the outer surface of the fascia. The levator muscle of the thyroid is one or more muscular slips that occasionally connect the hyoid bone with the thyroid gland. These vestigial muscles are inconstant in occurrence, location, and innervation. They have been divided into anterior, lateral, and posterior levators.

Vascular Supply

The thyroid gland competes with the adrenal glands for having the greatest blood supply per gram of tissue. One consequence is that hemostasis is a major problem of thyroid surgery, especially in patients with toxic goiter.

Arteries

Two paired arteries, the superior and inferior thyroid arteries, and an inconstant midline vessel, the thyroid ima artery, supply the thyroid .

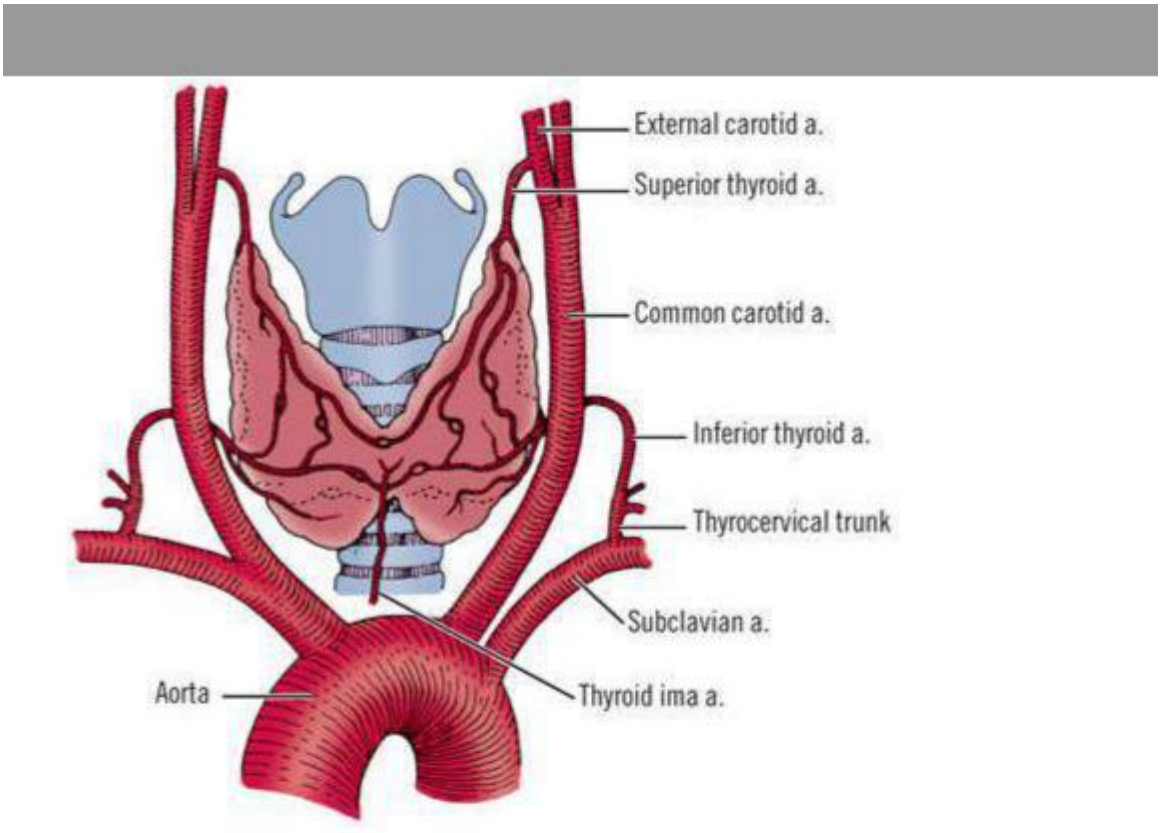
Superior Thyroid Artery

The superior thyroid artery arises from the external carotid artery just above, at, or just below the bifurcation of the common carotid artery. It passes downward and anteriorly to reach the superior pole of the thyroid gland. In part of its course, the artery parallels the external branch of the superior laryngeal nerve which supplies the cricothyroid muscle and the cricopharyngeus muscle, the lowest voluntary part of the pharyngeal musculature.

There are six branches of the superior thyroid artery - the infrahyoid, sternocleidomastoid, superior laryngeal, cricothyroid, inferior pharyngeal constrictor, and terminal branches of the artery for the blood supply of the thyroid and parathyroid glands.

Usually there are two branches to the thyroid —the anterior and posterior— but occasionally there may be a third, the so-called lateral branch.

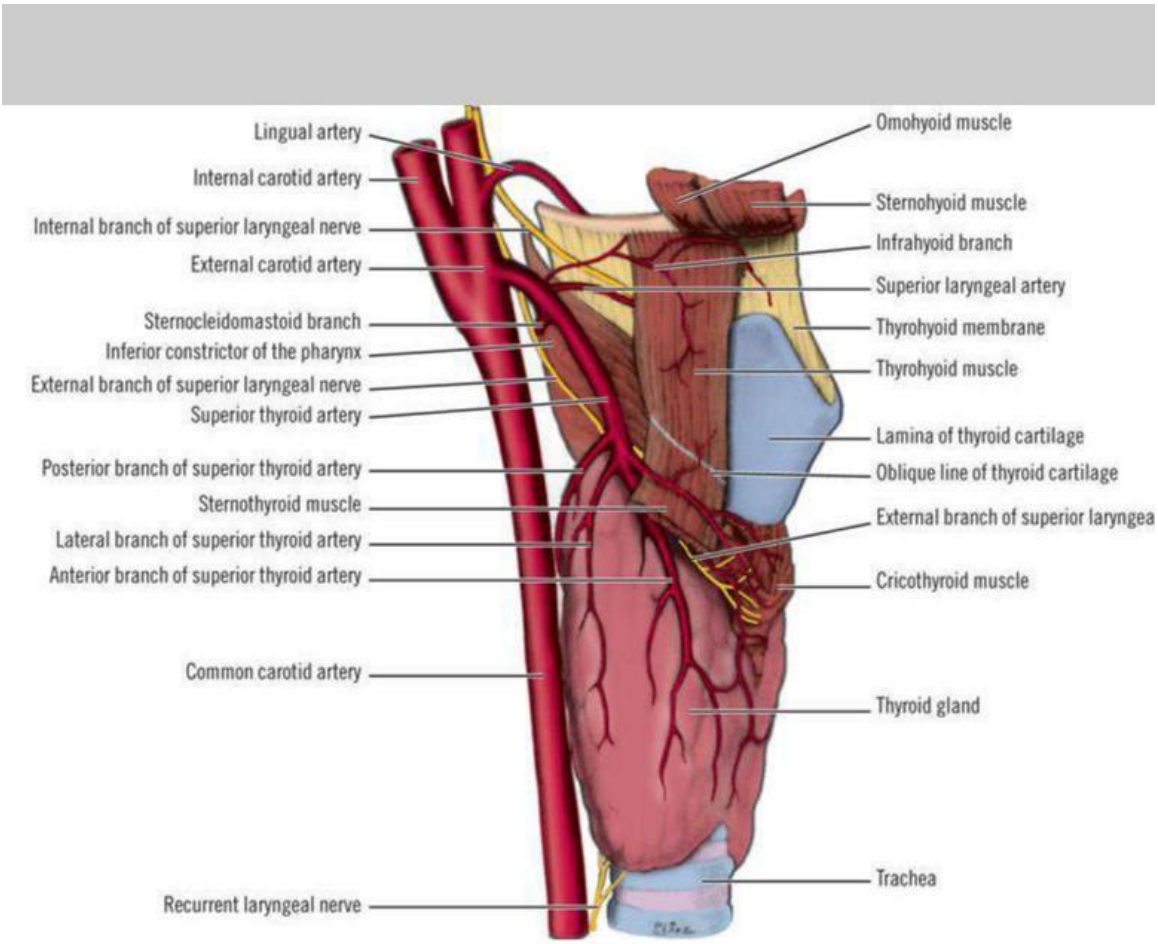
The arterial supply of thyroid gland



At the superior pole, the superior thyroid artery divides into anterior and posterior branches. The anterior branch anastomoses with the contralateral artery; the posterior branch anastomoses with branches of the inferior thyroid artery. From the posterior branch, a small parathyroid artery passes to the superior parathyroid gland.

In a study of thyroid glands removed at autopsy from Japanese patients, observed that an anastomosing vessel from the posterior branch of the superior thyroid artery supplied the superior parathyroid in 45% of cases. The majority of 92 glands (67%) had a single artery of supply; 1/3 had two or more small vessels which entered the gland. In the photographs of the specimens, the branching pattern of the primary vessel supplying the gland appeared to indicate that its origin was from the superior thyroid artery.

Branches of superior thyroid artery



Inferior Thyroid Artery

The inferior thyroid artery usually arises from the thyrocervical trunk, but in about 15 percent of individuals it arises directly from the subclavian artery.

The inferior thyroid artery ascends behind the carotid artery and the internal jugular vein, passing medially and posteriorly on the anterior surface of the longus coli muscle. After piercing the prevertebral fascia, the artery divides into two or more branches as it crosses the ascending recurrent laryngeal nerve.

The recurrent laryngeal nerve may pass anterior or posterior to the artery, or between its branches . The lowest branch sends a twig to the inferior parathyroid gland and supplies

the lower pole of the thyroid gland. The upper branch supplies the posterior surface of the gland, usually anastomosing with a descending branch of the superior thyroid artery. On the right, the inferior thyroid artery is absent in about 2 percent of individuals. On the left, it is absent in about 5 percent . The artery is occasionally double.

Thyroid Ima Artery

The thyroid ima artery is unpaired and inconstant. It arises from the brachiocephalic artery, the right common carotid artery, or the aortic arch. It occurs in about 10 percent of individuals, according to Montgomery. It may be as large as an inferior thyroid artery or it may be a mere twig. Its position anterior to the trachea makes it important in tracheostomy.

Veins

Veins of the thyroid gland form a plexus of vessels lying in the substance and on the surface of the gland. The plexus is drained by three pairs of veins, the superior, middle, and inferior thyroid veins

Superior Thyroid Vein

The superior thyroid vein accompanies the superior thyroid artery. Emerging from the superior pole of the thyroid, the vein passes superiorly and laterally across the omohyoid

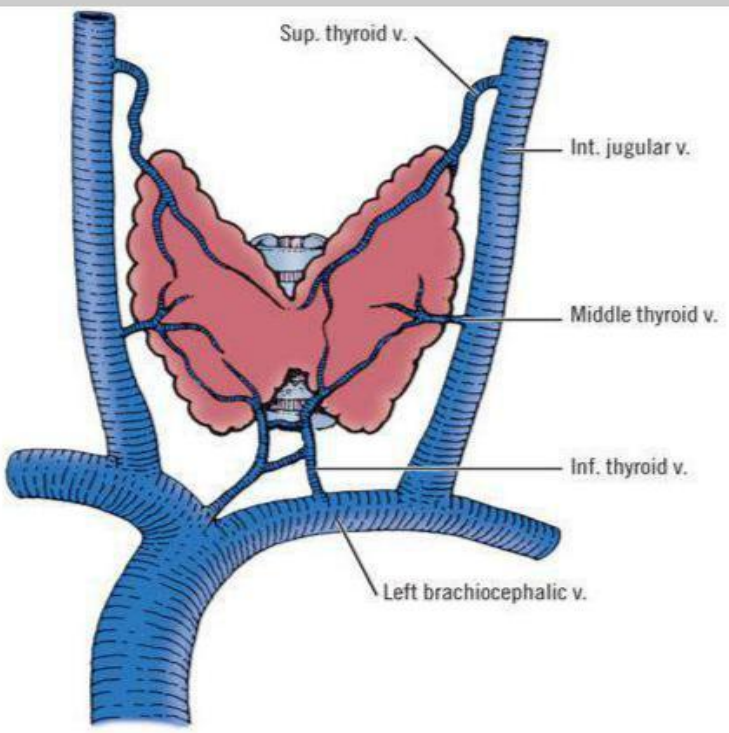
muscle and the common carotid artery to enter the internal jugular vein alone or with the common facial vein.

Middle Thyroid Vein

The middle thyroid vein arises on the lateral surface of the gland at about two-thirds of its anteroposterior extent. No artery accompanies it. It crosses the common carotid artery to open into the internal jugular vein. This vein may be absent or, occasionally, double. The extra vein is inferior to the normal one; it has been called the "fourth" thyroid vein. The importance of these middle thyroid veins is in their vulnerability during thyroidectomy.

Inferior Thyroid Vein

The inferior thyroid vein is the largest and most variable of the thyroid veins; the right and left sides are usually asymmetric. The right vein leaves the lower border of the thyroid gland, passes anterior to the brachiocephalic artery, and enters the right brachiocephalic vein. The left vein crosses the trachea to enter the left brachiocephalic vein. Rarely, the right vein crosses the trachea to enter the left brachiocephalic vein, sometimes forming a common trunk with the left vein. This common trunk is called the thyroid ima vein.



Venous drainage of the thyroid gland

Lymphatics

Several broad patterns of lymphatic drainage of the thyroid gland have been proposed . Each conceptualization is based on the same facts; each is correct. We will follow that of Hollinshead.

Patterns of Drainage

Median Superior Drainage

Three to six vessels arise from the superior margin of the isthmus and from the medial margins of the lateral lobes. These vessels pass upward in front of the larynx to end in the digastric lymph nodes. Some vessels may enter one or more prelaryngeal ("Delphian") nodes just above the isthmus. Secondary drainage may be to upper jugular nodes on either side or to pretracheal nodes below the thyroid by a vessel passing from the Delphian nodes downward over the front of the thyroid.

It has been suggested that there is a connection between the lymphatic drainage of the superior thyroid artery and the orbit by way of the jugular chain of cervical lymph nodes. In neither the orbit nor the eye itself can lymphatic vessels be demonstrated.

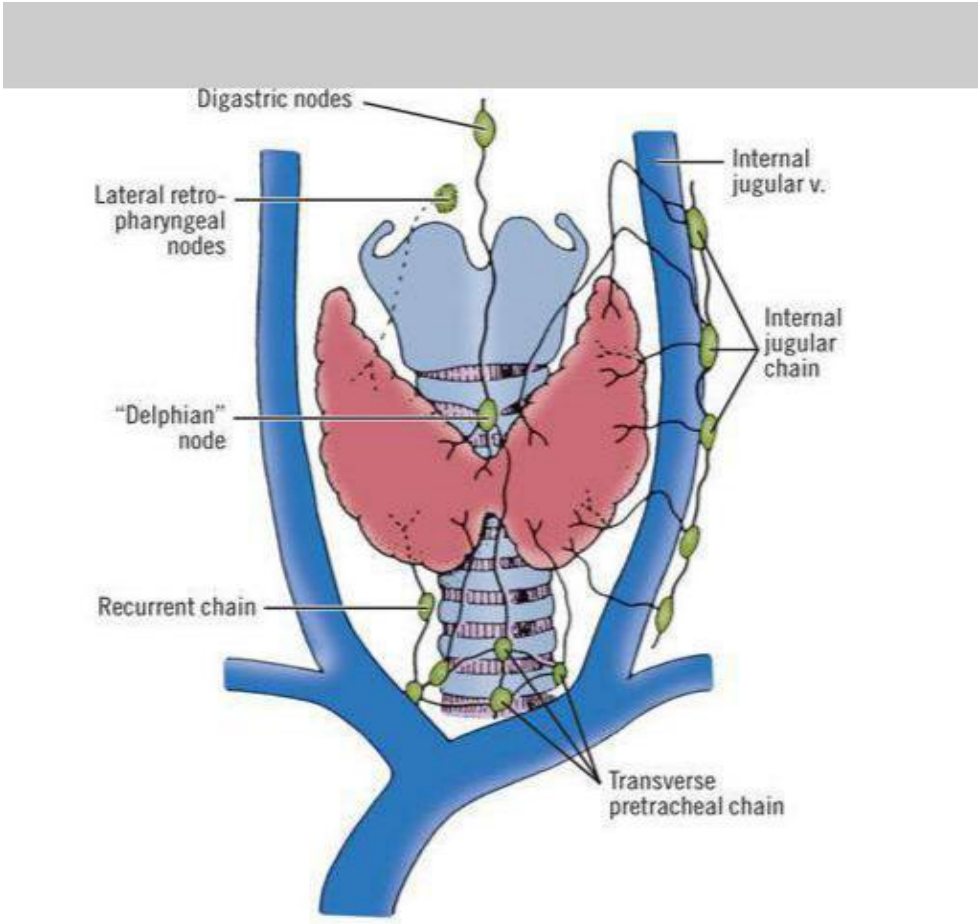
The immediate cause of exophthalmus associated with thyroid disease is the enlargement of the extraocular muscles, especially the inferior rectus and inferior oblique. Thyroid antigen or antigen-antibody complexes reaching the eye from the thyroid gland produce an autoimmune response in the extraocular muscles

Median Inferior Drainage

Several lymph vessels drain the lower part of the isthmus and the lower medial portions of the lateral lobes. They follow the inferior thyroid veins to end in the pretracheal and brachiocephalic nodes.

Right and Left Lateral Drainage

Lymphatic trunks arise from the lateral border of each lobe. Superiorly they pass upward with the superior thyroid artery and vein. Inferiorly they follow the inferior thyroid artery.. Between these two groups, some vessels pass laterally, anteriorly, or posteriorly to the carotid sheath to reach the lymph nodes of the internal jugular chain. Occasionally,such vessels drain into the right subclavian vein, jugular vein, or thoracic duct without passing through a lymph node.



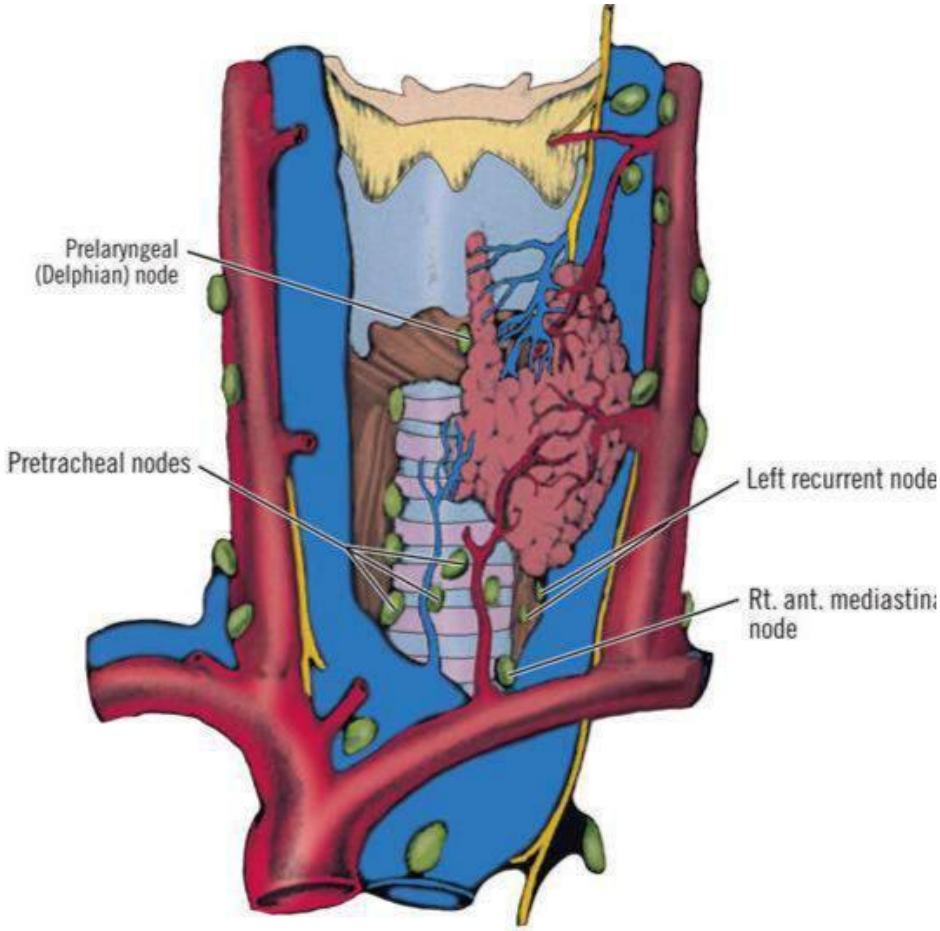
Lymphatic drainage of the thyroid gland

Posterior Drainage

Posterior lymphatic vessels arise from the inferomedial surfaces of the lateral lobes to drain into nodes along the recurrent laryngeal nerve. Occasionally, a posterior ascending trunk from the upper part of the lobe reaches the retropharyngeal nodes.

Metastatic Spread

A representation of lymph node regions of importance for management of thyroid carcinoma and Lymph node groups at the highest risk for regional metastasis from differentiated thyroid carcinoma are shown below.



LN regions of importance for thyroid carcinoma

Innervation

The thyroid gland is innervated by the sympathetic system from the superior, middle, and inferior ganglia of the cervical chain. But in thyroid surgery the recurrent and superior laryngeal nerves of the parasympathetic (vagus) system (which play no role in the innervation of the gland) are of utmost importance, so we consider them here.

Recurrent Laryngeal Nerves (Inferior Laryngeal)

Normal Anatomy

The right and left recurrent laryngeal nerves are intimately related to the thyroid gland. The right recurrent nerve branches from the vagus as it crosses anterior to the right subclavian artery. The right recurrent nerve loops around the subclavian artery from posterior to anterior, crosses behind the right common carotid and ascends in or near the tracheoesophageal groove. It passes posterior to the right lobe of the thyroid gland to enter the larynx behind the cricothyroid articulation and the inferior cornu of the thyroid cartilage.

The left recurrent nerve arises where the vagus nerve crosses the aortic arch, just distal to the origin of the left subclavian artery from the aortic arch. It loops under the ligamentum arteriosum and the aorta, and ascends in the same manner as the right nerve. Both nerves cross the inferior thyroid arteries near the lower border of the middle third of the gland.

Variations

Several variations may occur in the courses of the recurrent nerves. All serve to increase the possibility of injury to the nerve during thyroid surgery.In about 1 percent of patients, the right recurrent nerve arises normally from the vagus, but passes medially almost directly from its origin to the larynx without looping under the subclavian artery. In these cases, the right subclavian artery arises from the descending aorta and passes to the right behind the esophagus. This anomaly is asymptomatic, and the thyroid surgeon will rarely be aware of it prior to operation. Even less common is a nonrecurrent left nerve in the presence of a right aortic arch and a retroesophageal left subclavian artery.

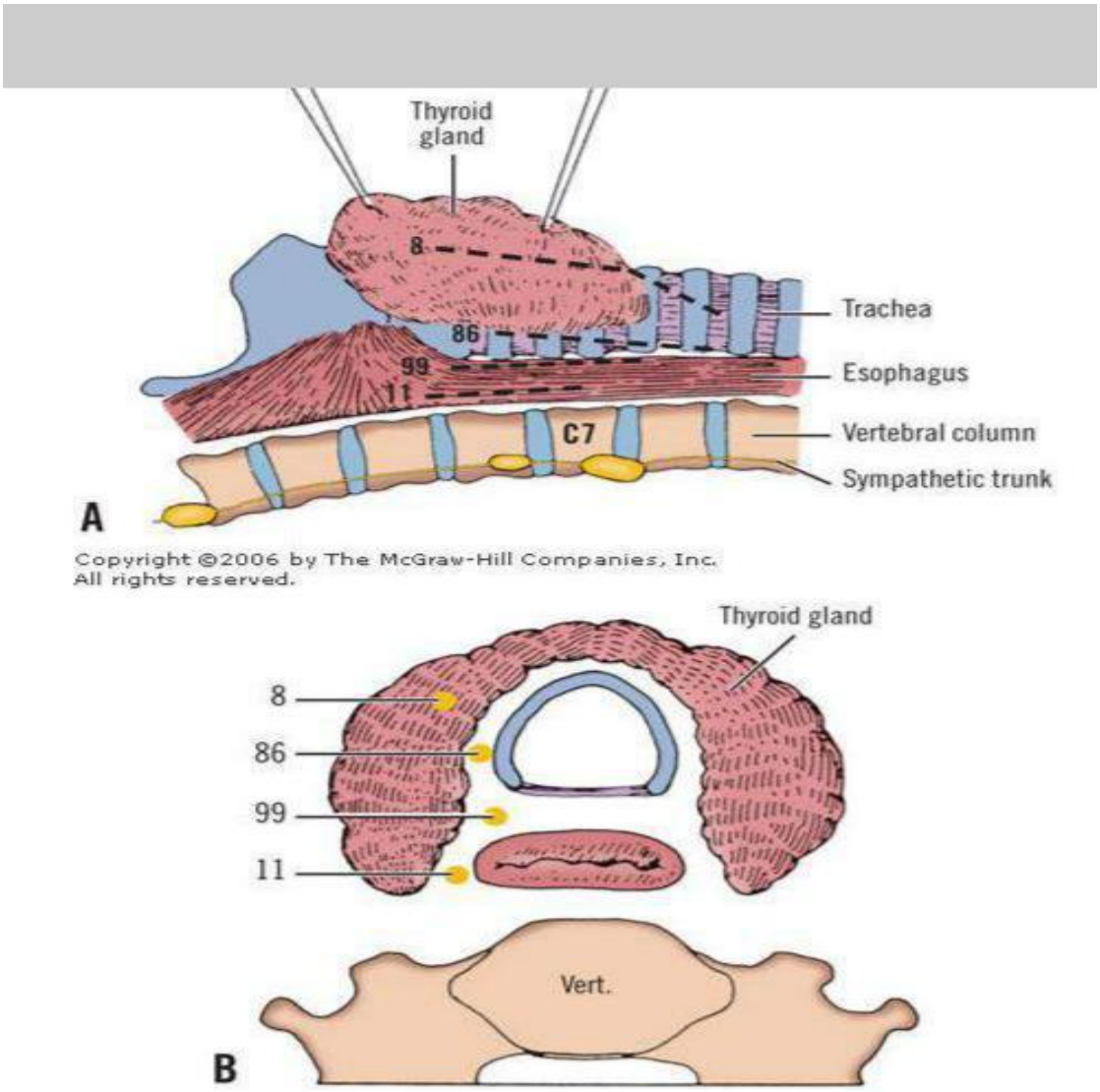
In the lower third of its course, the recurrent laryngeal nerve ascends behind the pretracheal fascia at a slight angle to the tracheoesophageal groove. In the middle third of its course, the nerve may lie in the groove, medial to the suspensory ligament of the thyroid gland (ligament of Berry), within the ligament, or within the substance of the thyroid

gland.The recurrent laryngeal nerve is safest and least visible when it lies in the tracheoesophageal groove. It is most vulnerable when it traverses the thyroid parenchyma. Where it runs in the suspensory ligament of the thyroid, it must be identified and protected before the ligament is divided.

The recurrent laryngeal nerve crosses the inferior thyroid artery at the middle third of the gland. It may lie anterior or posterior to, or between the branches of the artery. the secret to avoiding injury to the recurrent laryngeal nerve during thyroid surgery is as follows: (1) deep knowledge of the surgical anatomy of the thyroid region; (2) total extracapsular thyroidectomy; (3) a thorough search, identification, and exposure of the nerve itself; and (4) following the course of the nerve with care.

Superior Laryngeal Nerve

The superior laryngeal nerve arises from the vagus nerve just inferior to its lower sensory ganglion just outside the jugular foramen of the skull. The nerve passes inferiorly, medial to the carotid artery. At the level of the superior cornu of the hyoid bone it divides into a large, sensory, internal laryngeal branch and a smaller, motor, external laryngeal branch, serving the cricothyroid muscle and the cricopharyngeus. The point of division is usually within the bifurcation of the common carotid artery.



The course of recurrent laryngeal nerve at the thyroid gland.

Internal Laryngeal Nerve

The internal laryngeal branch pierces the thyrohyoid membrane with the superior laryngeal branch of the superior thyroid artery to enter and supply the larynx. The internal branch is rarely identified by the surgeon; identification occurs only in those cases where a greatly enlarged upper pole of the thyroid gland rises above the superior border of the thyroid cartilage . The internal laryngeal nerve provides general sensory fibers to the larynx and the area of the piriform recess of the laryngopharynx. It also provides parasympathetic fibers for the glandular elements and some taste fibers that supply taste buds around the epiglottis.

External Laryngeal Nerve

The external laryngeal branch, together with the superior thyroid vein and artery, passes under the sternothyroid muscles, posterior and medial to the vessels. The nerve then passes beneath the lower border of the thyrohyoid muscle to continue inferiorly to innervate the cricothyroid muscle. In addition to its contribution to phonation, the cricothyroid muscle plays a major role in the overall regulation of breathing by its control of expiratory resistance and flow. a branch of the external laryngeal nerve may also contribute to the innervation of the thyroarytenoid muscle and to the sensory supply of the vocal fold of the larynx. They postulated that the communicating branch of this nerve might represent the nerve of the 5th embryonic branchial arch.

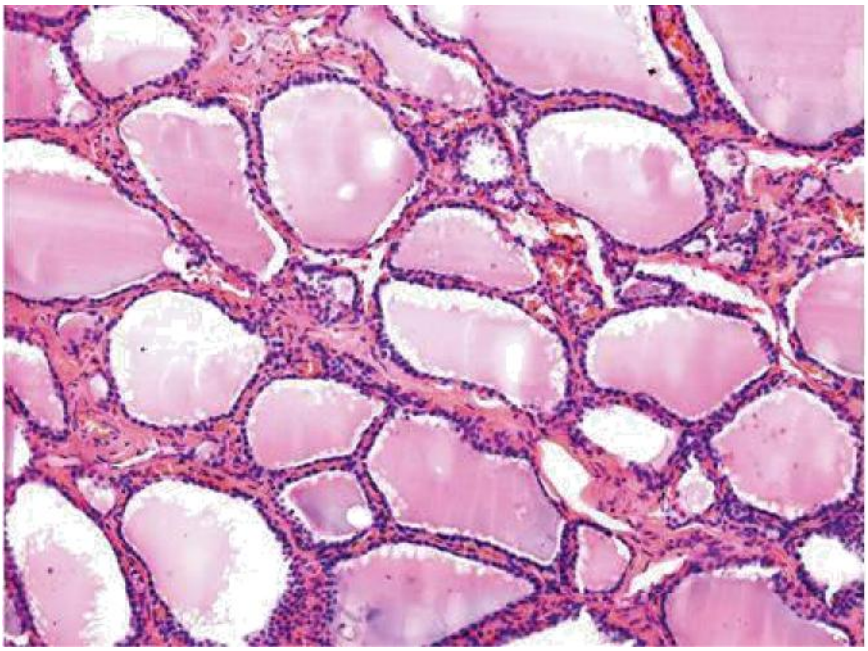
HISTOLOGY

The thyroid gland is surrounded by the thyroid capsule, which is a thin layer of connective tissue. From the capsule, several septa extend within the thyroid parenchyma, which is subdivided into several lobules. Epithelial cells (cuboidal or squamous) form the thyroid follicles; they are separated by thin connective stroma which is rich in both lymphatic and blood vessels. Small bundles of nerves are present.

There is a colloidal gelatinous collection in the center of the follicle. Each follicle has two types of cells: follicular and parafollicular, or C cells.

According to Ross and Reith, the follicular cells are responsible for the following actions: synthesis of thyroglobulin, iodination, storage of thyroglobulin, resorption of thyroglobulin, hydrolysis of thyroglobulin, and release of thyroid hormone into the blood and lymphatics.

The parafollicular, or C cells, can be found in the connective stroma between the follicles or in the follicular epithelium. Characteristically, they contain several secretory granules.



PHYSIOLOGY

The thyroid gland weighs 20 to 25 g in normal adults and is responsible for the production of two families of metabolic hormones, the thyroid hormones, thyroxine (T4) and triiodothyronine (T3), and the calcium-regulating hormone, calcitonin. The spherical thyroid follicular unit is the important site of thyroid hormone production. The follicular unit is made up of a single layer of cuboidal follicular cells that encompass a central depository of colloid filled mostly with thyroglobulin (Tg), the protein in which T4 and T3 are synthesized and stored.

Iodine Metabolism

Iodine is essential for the production of thyroid hormones. It can be efficiently absorbed from the gastrointestinal (GI) tract in the form of inorganic iodide and rapidly enters the extracellular iodide pool. The thyroid gland is responsible for storing 90% of total body iodide at any given time, with less than 10% existing in the extracellular pool. Iodide is stored in the thyroid as preformed thyroid hormone or as an iodinated amino acid. Iodide is transported from the extracellular space into the follicular cells against a chemical and electrical gradient via an intrinsic transmembrane protein located in the basolateral membrane of the thyroid follicular cells. Once inside the cells, iodide rapidly diffuses to the apical surface, where it is quickly moved to exocytic vesicles. Here, it is rapidly oxidized and bound to Tg. Transport of iodide into follicular cells is regulated by thyroid-stimulating hormone (TSH) from the pituitary gland, as well as by the follicular content of iodide. The relationship between iodine ingestion and thyroid disease has been known for more than 100 years. At the turn of the 20th century, the practice of iodine supplementation of food and water came about as a result of careful study in areas in which iodine insufficiency was found and linked to endemic goiter. Significant iodine deficiency still occurs in various undeveloped parts of the world. Iodine deficiency can result in nodular goiter,

hypothyroidism, and cretinism, and possibly the development of follicular thyroid carcinoma (FTC)

Thyroid Hormone Synthesis

Once organic iodide is efficiently oxidized and bound, it couples to Tg with tyrosine moieties to form iodotyrosines in a single conformation (monoiodotyrosine [MIT]) or a coupled conformation (diiodotyrosine [DIT];). The formation of DIT and MIT is dependent on an important intracellular catalytic agent, thyroid peroxidase, which has been well characterizedand is an integral part of the initial process of organification and storage of inorganic iodide. This enzyme, along with Tg, is remarkably specific to the thyroid follicular cells, making bothimportant in the diagnosis and management of autoimmune thyroid disease and well differentiated thyroid cancer. MIT and DIT are biologically inert. Coupling of these two residues gives rise to the two biologically active thyroid hormones, T4 and T3. T4 is formed by the coupling of two molecules of DIT, whereas T3 is formed by the coupling of one molecule of MIT with one molecule of DIT. In normal circumstances, formation of T4 predominates. Both T3 and T4 are bound to Tg and stored in the colloid in the center of the follicular unit, which allows quicker secretion of the hormones than if they had to be synthesized de novo. This rapid and metabolically active process normally results in the storage of about 2 weeks' worth of thyroid hormone in the organism under normal circumstances. Most thyroid hormone released from the thyroid gland is T4, which is deiodinated in peripheral extrathyroidal tissues and converted to T3. Release of T4 and T3 is regulated by the apical membrane of the follicular cell via lysosomal hydrolysis of the colloid that contains the Tg-bound hormones. The apical membrane of the thyroid cell forms multiple pseudopodia and incorporates Tg into small vesicles, which are then brought into the cell apparatus. Within the vesicles, lysosomal hydrolysis results in the reduction of the disulfide bonds and T3 and T4 are then free to pass through the basement membrane and be absorbed into the circulation, where more than 99% of each hormone is bound to serum proteins. This metabolic process is

efficient in releasing T3 and T4 while maintaining the storage components, Tg and colloid, within the follicular apparatus. Although sensitive assays of peripheral blood can measure Tg, peripheral Tg represents an extremely small fraction of total body stores. Residual iodotyrosines undergo peripheral breakdown, deiodination, and recycling and can then be added to the recently absorbed iodide stores and become available for the synthesis of new thyroid hormone .

Thyroglobulin

Tg is a 660-kDa glycoprotein specific to the follicular cell that is the primary component of the colloid matrix necessary for iodination and hormonogenesis. Tg facilitates theconversion of MIT and DIT into T3 and T4. This process is accompanied by the escape of small amounts of Tg into the peripheral bloodstream, where it can be assayed. TSH enhances the whole process of endocytosis, proteolysis, and release through an adenylate cyclase system. Excess peripheral levels of iodine inhibit further release by enhancing Tg resistance to proteolysis. Peripheral Tg can be measured to evaluate benign or malignant thyroid neoplasms. Measurement of peripheral Tg has predictive value for the recurrence of well-differentiated thyroid carcinoma, locally or in metastatic deposits after initial total thyroidectomy. However, the usefulness of measuring serum Tg levels prior to the initial resection of a known or suspected welldifferentiated thyroid cancer is unknown and its routine measurement is not recommended.

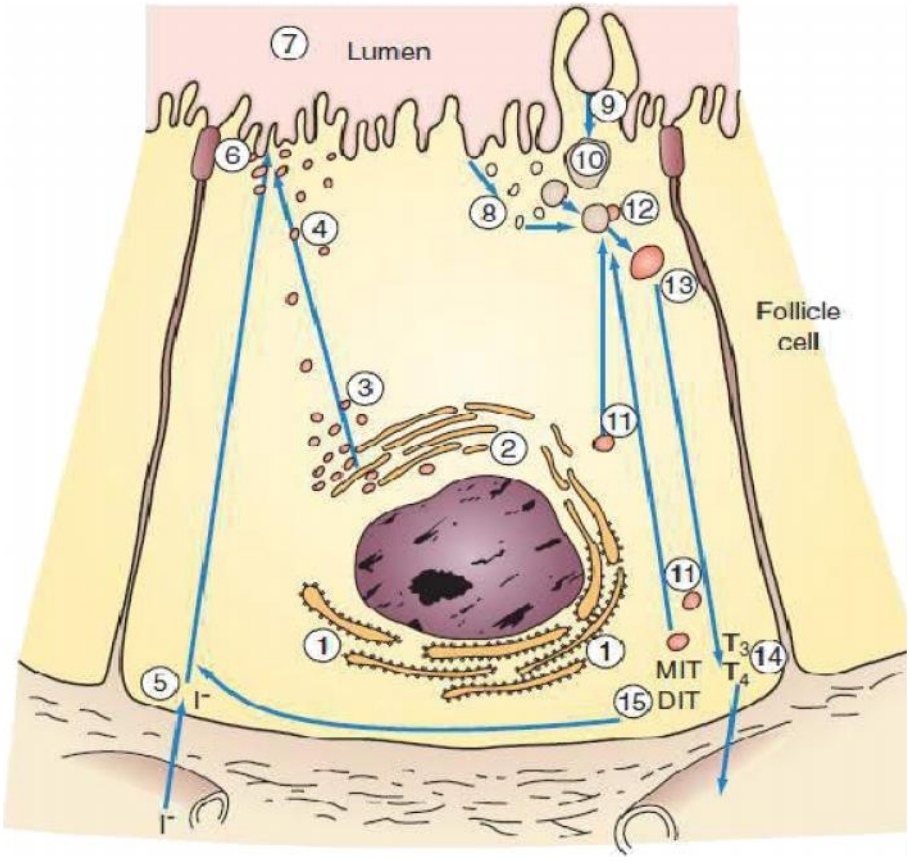


Fig – 14. Diagrammatic scheme of thyroid hormone formation and secretion. 1, Tg and protein synthesis in the rough endoplasmic reticulum. 2, Coupling of the Tg carbohydrate units in the smooth endoplasmic reticulum and Golgi apparatus. 3, Formation of exocytotic vesicles. 4, Transport of exocytotic vesicles with noniodinated Tg to the apical surface of the follicle cell and into the follicular lumen. 5, I odide transport at the basal cell membrane. 6, I odide oxidation, Tg iodination, and coupling of iodotyrosyl to iodothyronyl residues. 7, Storage of iodinated Tg in the follicular lumen. 8, Endocytosis by micropinocytosis. 9, Endocytosis by macropinocytosis (pseudopods). 10, Colloid droplets. 11, Lysosome migrating to the apical pole. 12, Fusion of lysosomes with colloid droplets. 13, Phagolysosomes with Tg hydrolysis. 14, T3 and T4 secretion. 15, MIT and DI T deiodination.

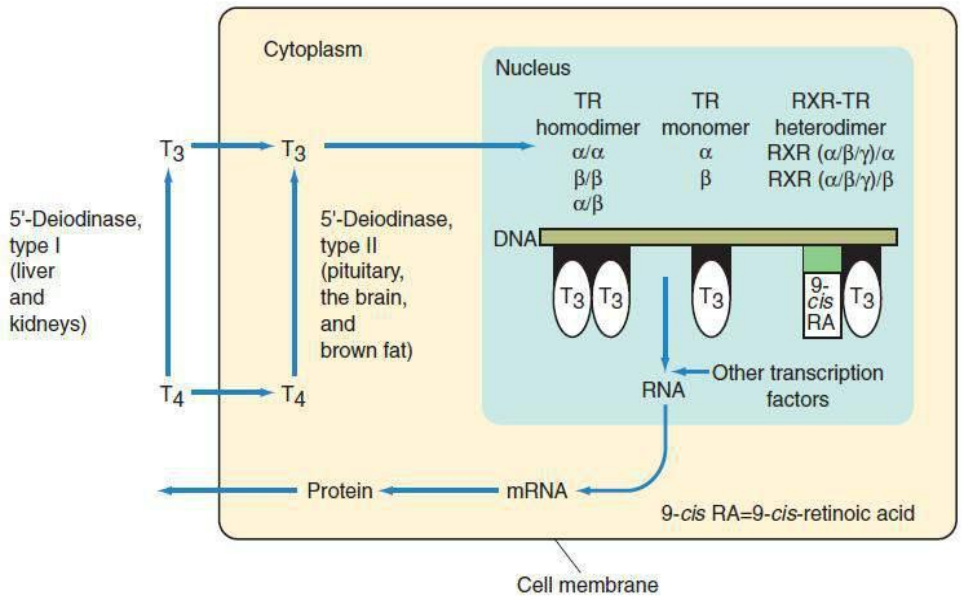
Regulation of Thyroid Hormone Secretion

The hypothalamic-pituitary-thyroid axis regulates thyroid hormone production and release in a classic endocrine feedback system. The major regulator of thyroid gland activity is the glycoprotein TSH, which is a major growth factor for the thyroid. TSHstimulates thyroid cell growth and differentiation, as well as iodine uptake and organification and release of T3 and T4 from Tg. Also, TSH has been shown to stimulate the growth and invasive characteristics of some well-differentiated thyroid cancer cell lines in vitro. TSH is a 28-kDa glycoprotein secreted in a pulsatile fashion by the anterior pituitary gland. It has two components; the α subunit is common to other anterior pituitary hormones but the β subunit is unique to TSH and determines the hormone's biologic specificity. Once TSH activates the receptor (TSH-R), it interacts with a guanine nucleotide–binding protein (G protein), stimulating the production of cyclic adenosine monophosphate (cAMP). This cAMP pathway is an important hormone-synthesizing event. Receptors coupled with G proteins have seven transmembrane-spanning domains, with cytoplasmic and extracellular loops. The first three of these cytoplasmic loops have important relationships in mediating the TSH-dependent increase in cAMP production and therefore in stimulating thyroid hormone production. The receptors that respond to TSH have been identified and cloned. Specific mutations in the genetics of this system have been identified and are associated with follicular thyroid neoplasms. The feedback loop is an important regulator of TSH secretion. Increased thyrotropin-releasing hormone (TRH) from the paraventricular nucleus of the hypothalamus and reduced levels of T3 stimulate release of TSH from the anterior pituitary. TRH is a three–amino acid peptide that passes through the hypothalamic portal system into the median eminence and through the pituitary stalk to the anterior pituitary. Peripheral thyroid hormone levels may, in addition to stimulating release of TSH from the anterior pituitary, enhance TRH secretion. Many pathologic states result in increased peripheral levels of T3 and T4, which decrease TSH secretion by a negative feedback loop. Peripheral T4 is locally

deiodinated in the pituitary and converted to T3, which then directly inhibits the release and synthesis of TSH. The condition that usually decreases TSH secretion is classified as primary hyperthyroidism. It has many causes, including many types of thyroiditis, Graves' disease, autonomously functioning thyroid nodules, and conditions that increase human chorionic gonadotrophin (hCG) levels, such as gynecologic malignancies and overuse of exogenous thyroid hormone. Decreased levels of TSH can also be caused by abnormalities at the level of the pituitary and/or hypothalamus, which are collectively termed *central hypothyroidism.* These conditions are much rarer than primary hyperthyroidism. Although TSH is the primary regulator of thyroid hormone synthesis, intrinsic autoregulatory mechanisms are alternative routes whereby the thyroid can control intraglandular stores of thyroid hormones. In areas in which dietary iodide is excessive, the thyroid gland has an autoregulated process that inhibits the uptake of iodide into follicular cells. The reverse is true in iodide deficiency. Excessively large doses of iodide have complex effects. These include an increase in organification followed by cessation of production, a syndrome known as the Wolff- Chaikoff effect.

Peripheral Action of Thyroid Hormones

In the periphery, T3 is significantly more potent than T4. Most T4 is converted to T3, which has a high affinity for the peripheral nuclear thyroid hormone receptor (TR), a member of the steroid hormone receptor family. Therefore, the action of thyroid hormones in the periphery consists predominantly of the interaction of T3 with the nuclear TR, which then binds to regulatory regions in various gene-regulated processes. Two genes regulate TR production and activity, the α and β forms, which are located on chromosomes 17 and 3 . The β form of TR is contained within the liver; the central nervous system contains predominantly an α form of TR.



Cellular and molecular events involved in thyroid hormone function. T4 is converted in the periphery and in the cytoplasm of the cell into T3. T3 travels to the nucleus, where it binds to the thyroid hormone receptor (TR; homodimer, monomer, or heterodimer). TR binding leads to R NA transcription in association with other transcription factors; messenger R NA is subsequently expressed and then translated into protein.

The clinical result of thyroid hormone action is regulated through TR and its effect on various genes, expressions of which are then regulated in the nucleus via the production of polypeptides. For example, T3 acts on the pituitary by regulating transcription of the genes for the α and β subunits of TSH, which results in TSH secretion. T3 affects cardiac contractility by regulating the transcription of myosin heavy chain production in cardiac muscle. Of circulating T3 and T4, 80% is bound to thyroxinebinding globulin (TBG) in the periphery. A number of medications and clinical scenarios alter serum levels of TBG or the affinity of TBG for circulating thyroid hormone .

Also, T4 is bound to prealbumin and albumin. In pregnancy and other clinical situations with elevated estrogen levels, such as oral contraceptives, menopausal estrogen replacement therapy, and tamoxifen or raloxifene use (selective estrogen receptor

modulators), TBG levels are significantly increased, thereby resulting in higher levels of bound T4 (total) in the periphery. Other causes of increased TBG concentrations include heroine or methadone use, clofibrate, and 5-flurouracil (chemotherapeutic agent). In contrast, decreased TBG levels are caused by agents such as anabolic steroids (testosterone), nicotinic acid, and corticosteroids.

Such states are clinically euthyroid, however, because free T4 levels are not altered. Most T3 and T4 are bound to the extent that free T4 constitutes less than 1% of peripheral hormone. The bound form of thyroid hormone cannot pass from the extracellular space and must be in the free form to diffuse into extracellular tissues to affect major metabolic activity. T3 is especially important in this regard. The process whereby T3 and T4 dissociate from binding protein and diffuse into extracellular tissues is an efficient process that allows tight control of peripheral metabolic activities. Most T3 isperipherally derived from the deiodination of T4, which takes place largely in the plasma and liver. Other deiodination processes are found in the central nervous system, especially the pituitary gland and brain tissues, as well as in brown adipose tissue. Peripheral conversion of T4 to T3 can be impaired in many clinical circumstances, such as overwhelming sepsis and malnutrition, thionamide (propylthiouracil) use, high-dose corticosteroids, beta blockers, iodinated contrast agents, and amiodarone use . The half-life of T3 is approximately 8 to 12 hours and free levels disappear rapidly from the peripheral circulation. In adults, the half-life of T4 is approximately 7 days because of the efficient and significant degree of binding to carrier proteins. Therefore, thyroid hormones generally have a slow turnover time in the peripheral circulation and the body is ensured of at least a 7- to 10-day supply of T4 available for peripheral metabolism. A number of medications are known to stimulate the degradation of thyroid hormone .

Inhibition of Thyroid Synthesis

Drugs Antithyroid medications are an option for the treatment of thyroid excess states. The thionamide class of antithyroid drugs includes propylthiouracil (PTU) and methimazole (Tapazole). This class of drugs acts by inhibiting the organification and oxidation of inorganic iodine, as well as by inhibiting linkage of the initial iodotyrosine molecules MIT and DIT. In addition to these effects, PTU inhibits the peripheral conversion of T4 to T3. Because of this added capability, PTU is a popular choice for the rapid treatment of hyperthyroid conditions.

Methimazole has longer activity and requires a single daily dose; it is the preferred agent in nonpregnant individuals. Both drugs can cause agranulocytosis but this occurs in less than 1% of cases. Other side effects include rash, arthralgias, neuritis, and liver dysfunction (potentially worse with PTU). Also, they can act in the periphery to inhibit the peripheral conversion of T4 to T3. This effectively lowers serum T3 levels, thus allowing steroids to be used as a rapid inhibitory agent for hyperthyroid conditions. Steroids can also lower serum TSH concentration. Patients with thyrotoxicosis have increased adrenergic stimulation. Although beta blockers do not directly inhibit thyroid hormone synthesis per se, they are valuable in controlling peripheral sensitivity to catecholamines by blocking their effects. Therefore, cardiovascular symptoms such as an increased pulse rate, tremor, and anxiety can be improved, but the hypermetabolic state can remain or progress with this treatment alone. Iodine Iodine, given in large doses after the administration of an antithyroid medication, can inhibit thyroid hormone release by altering the organic binding process (Wolff-Chaikoff effect). This stunning effect is transient, but iodine supplementation can be used to treat hyperactivity of the gland in preparation for surgery.

EPIDEMIOLOGY AND INCIDENCE

Disorder of thyroid including the 'Solitary nodule' occur worldwide, palpable thyroid nodule in Euthroid individual is common in clinical practice occurring upto 4% of general population, their incidence increase with age. Autopsy finding disclose even a higher incidence, most series reports an incidence of 5-10%,in postmortem series of persons in whom the nodule was previously undetected during life. However, clinical interest in the nodule is disproportionate to actual biological significance since majority will be related to multinodular goiter.

In contrast, however, a true solitary thyroid nodule, accounting for up to approximately 25% of clinically detectable solitary thyroid nodule is important both clinically and pathologically since although most of the case turn out be benign, 10-30% will harbour malignant neoplasm . The incidence of malignancy in solitary nodule who undergo surgery is increasing chiefly due to improved selection of patients for surgery.

SEX INCIDENCE:

Thyroid disorders are preponderantly confined to females in the ratio of 6:1 and this is due to variations of thyroid hormone demand during female reproductive function, physiological events such as puberty, pregnancy, lactation. Incidence of solitary nodule is also higher in females.But incidence of Malignancy in solitary nodule is more in men (26%) compared to female (9%)

AGE INCIDENCE:

Thyroid nodules occur at all ages, the reported age range from 15-69 years with maximum incidence in 30-40 years. Solitary nodule is rare in children, the incidence of carcinoma in such a nodule under 25 years of age is about 50% and 75% in patient under 15 years.

INCIDENCE OF MALIGNANCY IN SOLITARY NODULE OF THYROID:

Though commonest cause of solitary nodule is not carcinoma, a significant proportion is carcinomatous. In general between 10-20% of solitary nodule removed surgically is malignant.

Solitary nodule found in thyroid of patient less than 20 years and greater than 60 years carries far greater risk of being malignant. Solitary nodule of thyroid can arise from diverse causes. The common causes of solitary thyroid nodules are adenomatous goiter, neoplasm and chronic thyroiditis.

The aetiology of the nodule depends upon the population under study, sex , age of patient and prior history of exposure to ionizing radiation.

In practice, a clinical diagnosis of solitary thyroid nodule is, in fact, a dominant nodule of multinodular goiter is 50% of cases , as shown on subsequent investigations any dominant nodule within a multinodular goiter should be essentially treated as solitary thyroid nodule , as they have incidence of malignancy of around 10%.

AETIOLOGICAL FACTORS

A- Aetiology of adenomatous nodules:

Adenomatous goiter occur as a result of compensatory mechanism against deficient synthesis of thyroid hormone by the thyroid gland. The hormone by the thyroid follicles is regulated by TSH, secreted by anterior pituitary which in turn is regulated by negative feedback mechanism by the levels of thyroid hormone in blood and by TRH sercreted by hypothalamus. When there are low levels of T3 and T4 in blood they stimulate anterior pituitary to secrete TSH , which acts on follicular cell, induces hyperplasia, and hypertrophy to trap iodine and synthesis more of T3 andT4 . The hyperplasia may not occur uniformly, several foci of hyperplasia may result ,of which some are large, some small. Following hyperplasia there is involution after need for T3and T4 decrease . Repeated stimulation of thyroid causes hyperplasia and involution of varying degrees end also degenerative changes and fibrosis resulting in nodularity. If among various nodule only one of them attain large size which cannot be detected clinically, a solitary adenomatous nodule ensues.

Iodine deficiency in endemic area results in endemic area results in highest incidence of goiter and greater than 50% prevalence is found in extreme iodine deficient area. Iodine deficiency alone always does not cause goiter. There is unusual geographic distribution of goiter with some areas more severely affected than other

B) AETIOLOGY OF THYROID NEOPLASMS:

a) Radiation: The relationship between ionizing radiation and development of benign adenomas and malignant tumors is well known. Thyroid exposure to radiation can occur in two ways.

External sources

Internal source.

External exposure can be because of medically administered external beam radiationor environmental exposure previously related to nuclear weapons attack or weaponstesting and more recently nuclear power plant accidents.

Internal injection of isotopes of iodine which is concentrated inthe thyroid gland can come from the ingection of the isotopes and from thefallout of nuclear weapons , explosion or power plant accitents.

The carcinogenic radiation is by 2 mechanisms

1. Cellular injury with altered cell division and replication of nucleic acids.
2. The injured cells produce less thyroid hormone leading to TSH stimulation which is itself cardiation exposure include:

a) Amount of radiation received

b) Duration of radiation received

c) Age at which radiation was received

d) Latent period

Low dose radiation for Tinea capitis (6-5 cGy), thymic enlargement (100 to400 cGy), enlarged tonsils and adenoids (750Egy) Acne vulgaris (200 to 1500 cGy) are best known etiological factor . The risk increases linearly from 6.5 to 2000 cGy, beyondwhich the incidence decline as radiation causes destruction of thyroid tissues. The risk maximum 20 to 30 years after exposure. Approximately 30% of exposed children develop thyroid nodules and of these estimated 30% are malignant.

B) Ingestion of radioisotopes and malignancy :

The most common exposure is due 131 I administered for diagnostic thyroid scans. A typical scan exposes the thyroid to approximately 50 rads of external beam radiation. Studies have shown that is only a small increase in the of incidence of malignancies of thyroid after exposure to this dose.

A more dangerous type of ingestion of radioisotopes comes from exposure to nuclear fallout . contrary to medically administered 131 I and short lived radio - isotopes such as 129 I and 131-135 I.

Vast majority of patients developing post radiation malignancy have papillary histology.

c) Diet

There is an increased incidence of follicular cancer in iodine deficient endemic

goiterous areas as well as an papillary carcinoma in iodine rich regions.

d) Sex:

Factors such as parity, early menopause, contraceptive use and late age at first birth in female population have been reported to have increased risk of thyroid carcinoma but the data been inconsistent.

The thyroid nodule is more likely to be a cancer in men than in men than in women and in young (under 20 years) and older (over 60 years) patients rather than others.

e) Genetic predisposition:

There is no clear familial syndrome or genetic dis ease associated with non-medullary thyroid carcinoma.

Loose associations with familial polyposis of colon including Gardner's syndrome, Cowden's syndrome, melanomas, testicular and bladder cancer have been reported. This contrasts with medullary thyroid carcinoma, which has a variety of genetic syndromes now being defined at molecular levels. The familial medullary carcinoma syndromes is transmitted as an autosomal dominant trait and thus 50% of the offspring would be expected to have this disease

C) Aetiology of chronic thyroiditis (Hashimoto's thyroiditis):

Hashimoto's thyroiditis is clearly autoimmune in nature and may be the most common autoimmune disorder as well This occurs as a painless diffuse goiter in young or middle age women and often presents as an incidental finding during routine physical examination.

PATHOLOGY

1) Colloid (adenomatoid) nodule:

This goiter is mainly due to stimulation with increased TSH. THS secretion is increased due to low level of circulating thyroid hormones. Simple goiter are more common in females than in males owing to the presence of estrogen receptors in thyroid tissue. Persistent growth stimulation causes diffuse hyperplasia, all lobules are composed of active follicles and iodine uptake is uniform. If TSH stimulation ceases, the goiter may regress. The goiter is soft diffuse and may become large enough to cause discomfort. A colloid goiter is a late stage of diffuse hyperplasia when TSH stimulation has fallen off and follicle are inactive and full of colloid.

Latter as a result of fluctuating stimulation of TSH, a mixed pattern develops with areas of active lobules and areas of inactive lobules. Active lobules become more vascular and hyperplastic until hemorrhage occurs, causing central necrosis and leaving only a surrounding rim of active follicle. Necrotic lobules coalesce to form nodules filled either with iodine – filled colloid or mass of new but inactive follicles.

Continual repetition of this process result in a nodular goiter. Most nodules are inactive and active follicles are present only in the internodal tissue.

Nodules are usually multiple forming a multinodular goiter. A toxic multinodular goiter usually develops in a large, long standing multinodular goiter of atleast 10 year duration, only one macroscopic nodule is found but microscopic changes will be present throughout the gland, this is one form of clinically solitary nodule. Nodules may be colloid, cellular and cystic degeneration and haemorrhage are common.

Adenomatous nodule:

Gross appearance: surface appears nodule , many times more than single nodule may be detected, cut surface usually shows a circumscribed nodule, Ranging from half a centimeter several centimeter ton several centimeters in diameter.

Adenomatous goiters are known to undergo cystic change . Focal haemorrhage, fibrosis and calcification are common. Microscopy: Nodules appears as clusters of small active looking follicles within lobules. Some follicles become colloid cysts due loss of their walls . Focal areas of necrosis with collection of red cell s and macrophages laden with Hemosiderin is also seen.

CLASSIFICATION OF ADENOMAS

Adenomas can be classified into Follicular adenoma and its variants Paqillary adenoma and Atypical adenoma

a) **Follicular adenoma:**

Almost all thyroid adenoma show follicle formation to a varying degree; follicle adenoma are usually but may contain a variable amount of colloid; It is unknown whether follicular adenomas show transition over time. The most important clinically relevant fact about follicular adenomas is that many of these tumors cannot be reliably distinguished from follicular carcinoma on clinical, isotopic, USG or FNAC only reliable method of making distinction by careful histological for evidence of capsular or angio invasion.

Macroscopically:

Degenerative changes such as cyst formation and hemorrhage are common. It is difficult to differentiate between an adenoma and has a well demarcated capsule, it goes in favour of adenoma.

Microscopically :

Follicular adenomas show constant of follicles. Tumor is surrounded by fibrous capsule, that often contains wide vascular spaces. The tumour cells from large and small follicles which confine to the inner margin of the capsule. According to the size of follicles and the degree of follicle formation, follicular adenomas are further classified as

1. Colloid adenoma [macrofollicular adenoma]
2. Simple adenoma [normofollicular adenoma]
3. Fetal adenoma [microfollicular adenoma]
4. Hurthle cell adenoma [follicular adenoma of oxyphilic cell type]
5. Embryonal adenoma (trabecular adenoma)
6. Follicular adenoma of clear cell type a typical adenoma
8. Atypical follicular of clear cell type.
9. Toxic adenoma (Hyper-functioning adenoma)

Hurthle cell adenoma (Askanazy or Langhans tumor) :

Hurthle cell neoplasm are composed of large frequently polygonal, eosinophilic cells with an abundance of fine granular cytoplasm. They comprise approximately 4.5% to 10% of all primary epithelial thyroid tumor. Gross: It is grayish brown in colour and solid on cut surface The central hyaline scar so characteristic of fetal adenoma is absent Most of these have distinct capsule it may be focally cystic or haemorrhagic.

Microsopy :

It is composed of Hurthle cells approximately 10-15 microns in diametetr with abundant eosinophilic granular cytoplasm and distinct cell membrane and round to oval nuclei that are larger than the nuclei of normal follicular cells often containing one or more nuclear, cytoplasmic invagination and single or multiple homogenous electron dense bodies

within mitochondrial matrix. Hurthle cell is generally believed to be variant of, or arise from follicular cells within thyroid.

Hurthle cells are also associated with other non-neoplastic inflammatory conditions viz. thyroiditis, Grave's disease and nodular lesions of thyroid. In absence of any capsular or invasion on HPE, hurthel cell neoplasm should be considered benign.

Embryonal adenoma (trabecular adenoma):

These are the most poorly differentiated of the follicular group. It is fleshy and densely cellular composed of columns of small, closely packed polyhedral cells after growing in branching cords with to tendency towards follicle formation. They are very rare. It neither is present at birth nor does it arise from rests of immature tissue. It arise from definitive thyroid epithelium. The term only implies that there is resemblance of such lesion developing thyroid.

Toxic adenoma:

This lesion is a true follicular adenoma but has become autonomous and secretes excess of thyroxin to produce toxicity. Since these toxic nodules have capacity to grow and function, independent of trophic hormone, a neoplastic pathogenic basis for these lesions is preferable.

Gross:

These are circumscribed lesions, which may be solitary with a capsule. It may involve a part or whole of the lobe. The uninvolved tissue can be identified With features consistent with atrophy.

Micro :

Features are those of follicular adenoma cells, tend to be columnar withsmall and large follicles containing pale watery colloid.

b) Papillary adenoma:

Papillary adenoma is a very rare neoplasm composed of benign papillae with fibrous stroma but without capsular invasion. This tumor is often cystic and is sometimes referred to as papillary cystadenoma. This tumor should not be confused with an encapsulated papillary carcinoma. About 5% of papillary carcinoma are encapsulated without gross evidence of invasion.

Diagnosis of benign papillary adenoma should be made only if nuclei have slight or pleomorphism and an extensive search fail to demonstrate invasion of capsule, blood vessels of adjacent parenchyma. Some pathologists consider all papillary tumors as malignant, and it may be difficult to exclude invasion, some others refer this as follicular adenoma with papillary hyperplasia structures which prompt Confusion.

c) Atypical adenoma:

These are occasionally encountered, described as ground of tumor which display unusual icroscopic features such as cellular hyper-chromatasia, bizarre nuclei from squamous islands and spindle cell growth pattern. This comprises about 2-3%. Hazard establised that atypical adenoma have histologic architecture of carcinoma but have a benign behavior, he emphasized the importance of invasiveness and stated that encapsulated tumour without evidence of capsular or blood vessel invasion were benign.

Gross : These are solid and have fleshy appearence and completely defined by capsule. They lack the gelatinous or semi translucent character of usual adenoma they are firm to hard.

Micro: They are cellular with compactly arranged cells than other adenomas Hazard sub-classified them as;

Follicular type -clearly packed follicles.

Solid type- cells in sheets or columns

Alveolar type –Organised but solid.

Focal atypical type-In diffuse cellular mass.

It is important to rule out capsular or vascular invasion to confirm benignity. III)

Malignant neoplasms of thyroid :

Classification of malignant neoplasm of thyroid:

a) Well differentiated thyroid carcinoma

i) Papillary carcinoma

ii) Follicular carcinoma

b) Poorly differentiated thyroid carcinoma;

i) Hurthle cell carcinoma.

ii) Variants of papillary carcinoma:

Tall cell variant.

Insular variant.

Columnar variant.

c) Medullary carcinoma.

d) Undifferentiated (Anaplastic) carcinoma

e) Others (rare)

- Lymphoma
- Squamous cell carcinoma.

- Sarcoma

- Metastatic tumors.

a) Well deffeerentiated thyroid carcinoma:

i) Papillary carcinoma of the thyroid :

Papillary CA is the most common thyroid CA in both children and adults with incidence of 62%. It frequently presents in 4^{th} and 5^{th} decades with male to female ratio of 1:3 nearly over ¾ of malignant thyroid tumor in children and young adults for acne and tonsillitis have been shown to result in an increased incidence of well Differentiated papillary carcinoma at any time usually 5 years after exposure. There is convincing evidence for an increase in incidence in incidence of papillary carcinoma in Hashimoto's thyroiditis.

Multicentricity of primary tumour is the most important feature of this cancer. It spreads via intraglandular lymphatics within the most important feature of this cancer. It spreads via intragludular lymphatic within the thyroid gland and then to the subcapsular and pericapsular lymphnodes. In one large series, the disease was localized to the thyroid gland in 67% of cases, thyroid and Lymph nodes in 13%, and lymphnode alone in 20%.

Minimal or occult / microcarcinoma tumors are defined as tumours of 1cm or less in size. They are non-palpable and usually incidental finding at operative, histologic or autopsy examination. Occult papillary thyroid cancer is present in 2 to 36% of thyroid glands removed at autopsy.

Papillary carcinoma is associated with excellent prognosis (10 years survival rate is 95%).

GROSS: Papillary CA are usually non encapsulated hard, off white, sclerotic tumour with an irregular margin. Some are well encapsulated and resemble follicular adenoma. Macroscopic papillae or cyst formation may be present. On occasion, the carcinoma diffusely infiltrate the gland. At other times the carcinoma may be so small as to be discovered only incidentally in a microscope section from thyroid removed for an unrelated lesion. Multicentricity is present in 20-60% of cases depending on exclusiveness of sampling.

Micro: Histologic diagnosis is made on the basis of papillary architecture or characteristic nuclear features. True papillae have fibrovascular core and are generally lined by single row of overlapping nuclei. The nuclei of These have been designated ground glass nuclei, optically clear nuclei or orphon-annie nuclei. They are best appreciated on formatting fixed permanent sections. They are not seen on alcohol fixed fine needle aspirate smears and are occasionally and very focally seen on frozen section. Occasional sharply delineated intra nuclear cytoplasmic inclusions are seen in about half of papillary CA. They are more easily appreciated on touch imprints and fine needle aspirated smears than on formalin fixed sections.

Recently, there is increasing attention to grooved nucleus resulting from deep in folding of nuclear membrane along axis of nucleus. Like all other nuclear features, it is not 100% specific for papillary CA. Psammoma bodies-calcific areas that are laminated, (quite specific for papillary carcinoma)are seen in less than half of papillary CA and are rarely present in other thyroid lesions. They are believed to represent remains of dead papillae.

Diagnosis of papillary CA is not based on single criteria but on constellation of findings, in particular, papillary projecting into open spaces as well as clear nuclei with prominent nuclear groove and psammoma bodies. It is increasingly recognized that carcinoma partially or completely composed of follicles but having nuclear features characteristics of papillary carcinoma behave biologically as papillary carcinoma. They

usually have favourable prognosis and a propensity for lymph node metastasis than haematogenous dissemination as follicular carcinoma do. These carcinoma are now diagnosed as papillary carcinoma, and those with exclusive or near-exclusive follicular component are designated follicular variants of papillary carcinoma. Majority of papillary carcinoma have some follicular component.

Sub types of papillary carcinoma worthy of special mention include - Insular variant is a poorly differentiated tumor composed of solid clusters or nests of cells often containing microfollicles and has prognosis intermediate between typical anaplastic carcinoma and differentiated carcinoma .

Encapsulated papillary carcinoma are surrounded by thick or thin fibrous capsule and comprise 4- 14% of papillary carcinoma. They have much better prognosis than those with infiltrating margins.

The tall cell variant of papillary carcinoma is characterized by elongated tall cells with basally oriented nuclei. These have worse prognosis than usual papillary carcinoma, with higher incidence of extra thyroidal invasion, recurrence, distant metastasis and death.

The diffuse sclerosing variant of papillary carcinoma is also more aggressive. It diffusely involve one or both lobes and is associated with extensive sclerosis, numerous bodies, a focally solid pattern, and a lymphocytic infiltrate. Lymph node metastasis are present in most cases and pulmonary metastasis often occur.

Cervical lymph node metastasis are present in 37-54% of patients with papillary carcinoma. Indeed lymph node metastasis are found more frequently with small tumors probably as a reflection of patient presentation, lymph node involvement may overshadow the primary especially if it is microscopic size. Lymph node involved may be totally replaced by thyroid tissue, a circumstance which was earlier designated as replaced aberrant thyroid.

Nodal metastasis are more frequent in young. There is no difference in survival between patient regional nodes are uncommon and occur in 12-14% of papillary Carcinoma. Metastasis are usually to lung, mediastinum and less often to bone, brain. Reported mortality varies from 2 -11 %. The most important factors associated with poor outcome are patient age over 50 yrs at diagnosis, extra thyroidal extension, tumor size greater than 1.5cm, angio-invasion, male sex and possibly DNA aneuploidy. Relative proportion of papillary and follicular components, presence of squamous metaplasia, psomomma bodies and fibrosis do not correlate with prognosis.

ii) Follicular carcinoma:

It is the next most common thyroid carcinoma comprising 20-25%, incidence is less in iodine sufficient areas. They occur more commonly in women (F:M= 2.6:1), most often in middle aged or older individual. They tend to behave more aggressively than papillary carcinoma and have a lower survival rate. While lymph node metastasis are unusual, a significant number of patients initially present with or subsequently develop distant metastasis.

Gross: Follicular carcinoma are solid, fleshy tumor that unlike papillary carcinoma are rarely occult, larger tumor may have focal haemorrhage or necrosis.

Micro: Follicular carcinoma have a range of pattern similar to those found in follicular adenomas. They may be solid with little actual follicle formation, form trabeculae or cords or have micro follicles. The architectural pattern has no pleomorphic and usually do not show a marked increase in mitotic activity, multicentricity is much less common than papillary carcinoma. Follicular carcinoma have been divided into:

- encapsulated or minimally invasive carcinoma
- widely invasive carcinoma

Minimally invasive carcinoma are grossly and microscopically encapsulated and thus follicular adenoma. Grossly they are not as colloid rich as adenomatous nodules and some follicular adenomas. They are distinguished from follicular adenomas by presence of microscopic capsular or blood vessel invasion. It is generally agreed that cytologic atypia and increased mitotic activity in an encapsulated follicular neoplasm should not be used as basis for diagnosis of carcinoma in absence of capsular or vascular invasion. Capsular or blood vessel invasion is usually focal, and many sections are needed to be examined before this is demonstrated.

Widely invasiave carcinoma include non-encapsulated carcinoma and encapsulatedcarcinoma with marked vascular and thyroid invasion, which may be microscopically apparent.

Definition of capsular invasion varies among authors. Kahn and Perzin defined capsular invasion as presence of tumor in capsule beyond the main tumor mass. Evans defined it as tumor nests within capsule. While tumor nests within capsule might represent invasion, it could also represent entrapment within capsule of adenoma. Therefore, growth of tumor cells into capsule roughly perpendicular to main tumor mass is necessary to diagnose as capsular invasion.

The definition of blood vessel invasion also varies among authors. It is generally agreed that vessels should be in the capsule or outside the capsule rather than in the tumor itself, that the vessels should be of venous caliber and tumor thrombus should he attached to vessel wall or covered by endothelium.

The prognosis of patient with encapsulated minimally invasive carcinoma is much better than for those with widely invasive carcinoma.it is found that metastasis developed in 2-3% and 25% of patient with minimally and widely invasive carcinoma respectively and cumulative death rate at 10 years was 3% and 32% respectively. Other unfavorable

prognostic factor include age >50 years at diagnosis, size more than 4 cm extra thyroidal invasion and to less extent histologic differentiation. Presence of metastasis at time of diagnosis appears to be most un-favorable risk factor.

Unlike papillary carcinoma, regional lymph node metastasis are unusual and distant metastasis are much more common usually to be bone, lungs via hematogenous route. Metastasis and recurrence may be cytologically bland, even resembling normal thyroid, and may be histologically diagnosable as malignant only because of their location.

b) Poorly differentiated carcinoma:

i) Hurthle cell carcinoma: Hurthle cell carcinoma accounts for 3% of allthyroid malignancies is a subtype of follicular carcinoma that closely resembles follicular carcinoma. This occurs in older persons usually 60-70years of age. The tumor contains an abundance of oxyphilic cells or oncocytes. They differ from follicular carcinoma in that they are more often multifocal and bilateral (approximately 30%),usually do not take up RAI are more likely to metastasize to local nodes (25%) and distant sites and are associated with high, mortality rate.

Gross: The tumors are characteristically solid and well vascularized. Most are well encapsulated throughout, invasive tumors tend to grow into the parenchyma in a multinodular fashion than can be very deceptive in that it can be underinterpreted as nodular hyperplasia.

Micro: The pattern of growth may be follicular, trabecular or papillary. The former is most common. The follicles when large are separated by long and thin fibrovascular septa that stimulate papillae when cut tangentially

iii) Medullary carcinoma;

medullary carcinoma accounts for 5% to10% of thyroid malignancies.The malignancy involves the para follicular cells or c cells derived from neural crest cells. this can occur in sporadic cases as a part of MEN type 2A or 2B . sporadic cases are more common in women while familial cases are autosomal dominant and affect both sexes equally. In sporadic cases, the lesion usually within one lobe where as men involves upper halves of both lobes.

Medullary thyroid tumors secrete not only calcitonin and carcino-embryonic antigen (CEA) but also calcitonin gene related peptide (CGRP), histaminadases, prostaglandins E2 and F2a and serotonin. The calcitonin excess is not associated with hypocalcemia. The presence of both a mass and an elevated calcitonin level is diagnostic of medullary carcinoma. Calcitonin is more sensitive tumor marker but CEA is a better predictor of prognosis. Screening for pheochromocytoma with 24 hour urinary catecholamines is mandatory in any patient whose thyroid mass is suspected as being medullary thyroid carcinoma.

Medullary carcinoma invades locally and gives rise to metastsis in cervical and mediastinal lymph nodes(50%) and also in distant organs (15-25%) particularly in lung, liver and skeletal system.

Gross: The tumour is solid, firm and non-encapsulated but relatively well circumscribed and has a grey to yellowish cut surface.

Micro: The classic presentation is represented by a solid proliferation of round to polygonal cells of granular amphophilic cytoplasm and medium sized nucleus, separated by a highly vascular stroma, hyalinized collagen and amyloid. The nuclei resemble those of neuroendocrine tumours in other areas of body. They are usually round and stippled “pepper and salt” chromatin.

There are several historical variants which include

a. Enacapsulated - better prognosis.

b. Follicullar.

c. Papillary.

d. Small cell- worst prognosis.

e. Giant cell.

f. Clear cell .

g. Melanontic .

h. Oncocytic.

i. Squanous .

j. Amphicrine.

k. Paraganglioma like

Age <40yrs, female sex, association with MEN 2a, uniform cytology, abundant amyloid and tumor confined to the thyroid are pointers to favourable outcome, while association with MEN 2b, necrosis with in tumor and high mitotic activity are adverse features.

d) Anaplastic carcinoma:

Anaplastic thyroid carcinoma represent less than 1% of all thyroid malignancies. This occurs in 7^{th} or 8^{th} decade. It is most aggressive from with dysphagia, cervical tenderness and painful neck mass. Superior venacava syndrome can also be part of presentation regional lymph nodes are frequently enlarged. Distant metastases to lungs and bones are not uncommon

Gross: the tumour is bulky, locally invasive, with a firm, whitish apperrance withextensive intrathyroidal extension.

Micro: These carcinomas are poorly differentiated with varying combinations ofgiant cells, spindle cells, squamous cells and fibrosis. Mitotic figures are abundant as are necrosis and vascular invasion.

Lymphomas:

Lymphomas account for less than 1% of thyroid malignancies and most are of the non-B-cell type.

Secondaries in thyroid: can occur from

- Renal cell carcinoma
- malignant melanoma
- Bronchogenic carcinoma;
- Breast carcinoma

These are rare very in thyroid.

Thyroid cyst :

common cause colloid degeneration ,50% .there will be absence of epithelial lining. involution of follicular adenoma present like a cyst.30% of solid nodules are cystic.cyst formation is common in papillary carcinoma of thyroid surgery indicated in complex cyst and if the size of the cyst more than 4cm Aspiration yields altered blood but re-accumulation is frequent.

v) **Thyroiditis:**

Types of thyroiditis:

1. Chronic lymphocytic thyroiditis (Hashimoto thyroiditis).
2. Sub-acute lymphocytic thyroiditis or sporadic or silent thyroiditis or post-partum thyroiditis.

3. Sub acute granulomatous thyroiditis (de-Quervain's thyroiditis).

4. Acute suppurative thyroiditis.

5. Invasive fibrous thyroiditis(Riedel's thyroiditis).

1) Hashimoto 's thyroiditis :

This is clearly autoimmune in nature and may be the mostcommon autoimmune disorder as well. The disorder occurs as a painless diffuse goiter in young or middle aged women (30-50yrs). The hallmarks of this disorder are high circulating antibodies to thyroid peroxidase (thyroid microsomal antigen) 90%, thyroglobulin, antibodies against TSH receptors. Progressive immunologically mediated thyroid cell damage leads to goiter formation and thyroid gland failure. Euthyroid individuals with Hashimoto 's thyroiditis develop hypothyroidism at the rate of approximately 5% per year. Mild thyrotoxicosis (Hashitoxicosis) has been reported to be the initial manifestation in up to 5% of patients. Physical examination typically reveals, non-tender goiter, which is generally symmetrical, often with a palpable pyramidal lobe. Regional lymph node enlargement may be observed. Nodular thyroid disease frequently occurs in Hashimoto's thyroiditis.

Gross: The cut surface is friable, vaguely or distinctly nodular, yellowish gray andgreatly resembles a hyper plastic lymph node. Colloid is not clearly discernible. Necrosis and calcification are absent.

Micro: There is disruption of epithelial cells and remaning epithelial cell and remaningepithelial cell become large and show oxyphilic changes (Askanazy cells or Hurthle cells). Two main abnormalities are lymphocytic infiltration of the stroma and oxyphilic change of follicular epithelium. The lymphoid tissue is distributed within and around the lobes and it exhibits large follicles with prominent germinal center. Plasma cells, histiocytes and scattered intra-follicular multinucleated giant cells can be present.

2) Sub-acute granulomatous thyroiditis :

This disorder has a number of eponyms including **de Quervain's thyroiditis, giant cell thyroiditis, and sub-acute painful thyroiditis.** This occurs more commonly in 30 to 40 years old women. A virus (Mumpsvirus and an unidentified cytopathic virus) etiology has been implicated. This often follows an upper respiratory tract infection. The symptoms includes painful thyroid enlargement, pain radiating to patient's jaw, muscular aches, fatigue, fever and malaise. Sub-acute thyroiditis has been associated with adeno, Coxsackie, Epastein-Barr and influenza viral infections and has been reported after hepatitis B vaccination.

The acute phase consists of thyrotoxicosis caused by follicular destruction and leakage of preformed hormone from the gland lasts 3 to 6 weeks but may last longer. During this phase the erythrocyte sedimentation rate is marked elevated. The radioactive iodine uptake during the thyrotoxic phase is low. After the acute phase, a period of transient asymptomatic euthyroidism follows. Hypothyroidism may occur after several more weeks and may last for several months, the recovery phase follows when all aspects of thyroid function return to normal in 4 to 6 months. Hypothyroidism may be permanent in up to 5%of patients.

Gross: The gland is enlarged twice it's normal. In advanced stage, the involved areas are firm.

Micro: The areas of marked inflammation and granulomas containing foreign body giant cells are present. The granulomas are not very distinct and caseation necrosis is consistently absent. Areas of fibrosis are seen, usually in patchy distribution.

3) Acute suppurative thyroiditis:

Bacterial infections of thyroid are rare. It is more common in children and is often preceded by upper respiratory tract infection or otitis media. The resistance of the thyroid due to infection is due to protective mechanisms that include is (1) rich blood supply to and lymphatic drainage from the thyroid, (2) the high glandular content of iodine which may be bactericidal, (3) the separation of thyroid from other structures of the neck by fascial plane and complete protective fibrous capsule surrounding the gland. The most common predisposing factor to infections of the gland appears to be preexisting thyroid disease since simple goiter, nodular goiter, Hashimoto's thyroiditis or thyroid carcinoma has been observed in up to two thirds of women and half men with infections thyroiditis.

Bacterial infections (Staphylococcus aureus and streptococcus pyogenes) are the most common cause of infectious thyroiditis . Bacterial thyroiditis may occur either via spread from a distant focus through the bloodstream or lymphatic or by direct inoculation from contiguous focus.

4) Riedel's thyroiditis :

Riedel's thyroiditis, also known as Riedel's struma and invasive fibrous thyroiditis, is a rare disorder of unknown etiology that is characterized by extensive fibrosis of thyroid gland this affects mainly women between the ages of 30 to 60 yrs (F:M= 3 to 4:1) thyroid antibodies have been reported in up to 67% of painless goiter. The extensive fibrosis is progressive and may eventually cause compression of adjacent structures particularly to trachea and oesophagus.

Physical examination reveals a goiter often described as "woody " in texture . Most patients are euthyroid unless almost complete replacement of gland occurs resulting in hypothyroidism.

Gross : The gland the is asymmetrical and involves only localized areas of the thyroid gland. The affected portion is stony hard and cuts with great resistance. Dense fibrous tracts extend from thyroid capsule to adjacent muscle, so that at surgery, the tissue planes are obliterated.

Micro: Fibrous tissue, that is frequently extensively hyalinized completely replaces the area, is often directly infiltrated by this connective tissue. Gaint cells are absent. The inflammation present is patchy and mononuclear type, with a predominance of lymphocytes and plasma cells.

TNM Classification of Thyroid Tumors

Papillary or Follicular Tumors	
Stage	**TNM**
<45 y	
I	Any T, any N, M0
II	Any T, any N, M1
≥45 y	
I	T1, N0, M0
II	T2, N0, M0
III	T3, N0, M0; T1–3, N1a, M0
IVA	T4a, N0–1a, M0; T1–4a, N1b, M0
IVB	T4b, any N, M0
IVC	Any T, any N, M1
Medullary Thyroid Cancer	
Stage	**TNM**
I	T1, N0, M0
II	T2–3, N0, M0
III	T1–3, N1a, M0
IVA	T4a, N0–1a, M0; T1–4a, N1b, M0
IVB	T4b, any N, M0
IVC	Any T, any N, M1
Anaplastic Cancer	
Stage	**TNM**
IVA	T4a, Any N, M0
IVB	T4b, Any N, M0
IVC	Any T, Any M, M1

Definitions:

Primary tumor (T)

TX = Primary tumor cannot be assessed

T0 = No evidence of primary tumor

T1 = Tumor ≤2 cm in diameter, limited to thyroid

T2 = Tumor >2 cm but <4 cm in diameter, limited to thyroid

T3 = Tumor >4 cm in diameter, limited to thyroid, or any tumor with minimal extrathyroidal invasion

T4a = Any size tumor extending beyond capsule to invade subcutaneous soft tissue, larynx, trachea, esophagus, or recurrent laryngeal nerve, or intrathyroidal anaplastic cancer

T4b = Tumor invading prevertebral fascia, or encasing carotid artery or mediastinal vessels; or extrathyroidal anaplastic cancer Regional lymph nodes (N)—include central, lateral cervical, and upper mediastinal nodes

NX = Regional lymph nodes cannot be assessed

N0 = No regional lymph node metastasis

N1 = Regional lymph node metastasis

N1a = Metastases to level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes)

N1b = Metastases to unilateral, bilateral, or contralateral cervical or Superior mediastinal lymph nodes

Distant metastasis (M)

MX = Distant metastases cannot be assessed

M1 = No distant metastasis

CLINICAL FEATURES

HISTORY:

1) Swelling :

Most commonly patients present with a history of a slowly growing swelling which otherwise is asymptomatic. Sudden increase in size is suggestive of haemorrhage into the nodule. Recent increase in size is suggestive of malignancy.

2) Pain:

Some patients complain of vague pain in the nodule. Recent onset of sudden pain suggests haemorrhage into the nodule. Pain is also feature in Riedel ‘s thyroiditis. Pain is a late feature of malignancy which has invaded deeper structures.

3) Pressure symptoms:

a. History of hoarseness of voice, not due to upper respiratory disease, suggests malignant nature of the nodule because of malignant infiltration of recurrent laryngeal nerves. Rarely, a benign large nodule can press upon the recurrent laryngeal nerve leading to hoarseness of voice.

b. Pressure upon the trachea causes dyspnoea and on the oesophagus may cause dysphagia.

4) Symptoms of toxicity / hypothyroidism:

Toxic symptoms are seen in toxic adenoma, toxic adenomatous nodule and very rarely in functioning carcinoma. Symptoms common to most patients with hyperthyroidism include heat intolerance, increased sweating and thirst, and weight loss despite adequate caloric intake. Symptoms of increased adrenergic stimulation include palpitations, nervousness, fatigue, emotional lability, hyperkinesis, and tremors. The most common

gastrointestinal symptoms include increased frequency of bowel movements and diarrhea. Female patients often develop amenorrhea, decreased fertility, and an increased incidence of miscarriages.

The symptoms hypothyroidism. in general, are non-specific, they include tiredness, weight gain, cold intolerance, constipation, and menorrhagia. Patients with severe hypothyroidism or myxedema develop characteristic facial features as a consequence of the deposition of glycosaminoglycans in the subcutaneous tissues, leading to facial and periorbital puffiness. The skin becomes rough and dry often develops a yellowish hue from reduced conversion of carotene to vitamin A. hair becomes dry and brittle, and severe hair loss may occur .there is also a characteristic loss of the outer two-thirds of eyebrows. An enlarged tongue may impair speech, which is already slowed, in keeping with the impairment of mental processes. Untreated dementia may lead to myxedema madness. Patients may also have nonspecific abdominal pain accompanied by distention and constipation. Libido and fertility are impaired in both sexes.

5) Symptoms of metastasis:

In bones, lungs etc. may be seen in follicular, anaplastic and rarely papillary carcinoma. Lymph node metastasis may present as lateral neck swellings along with or thyroid swelling.

6) Diarrhea may be only symptom of medullary thyroid carcinoma

Family history :

Family history of thyroid swelling is usually seen in familial medullary thyroid carcinoma.

Past history:

Past history of neck irradiation is significant as it may lead to papillary carcinoma of thyroid.

PHYSICAL FINDINGS :

General physical examination helps to assess whether the patient is euthyroid, hypothyroid or hyperthyroid. It may reveal a metastatic site from a cancerous nodule of thyroid.

Patients with hyperthyroidism, on physical examination

- will have weight loss and facial flushing
- skin may be warm and moist and, African American patients often note darkening of their skin
- Tachycardia or atrial fibrillation is present, with cutaneous vasodilation leading to a widening of the plus pressure and a rapid fall off in the transmitted pulse wave (collapsing pulse), congestive cardiac failure may also be present
- A fine tremor, muscle wasting, and proximal muscle group weakness with hyperactive tendon reflexes are often present.

Patients with severe hypothyroidism or myxedema develop characteristic facial features as a consequence of the deposition of glycosaminoglycans in the subcutaneous tissues, leading to facial and peri-orbital puffiness skin becomes rough and dry and often develops a yellowish hue from reduced conversion of carotene to vitamin A

Hair becomes dry and brittle, and severe hair loss may occur

There also is a characteristic loss of the outer two-thirds of the eyebrows

Cardiovascular changes in hypothyroidism include bradycardia, cardiomegaly, pericardial effusion, reduced cardiac output, and pulmonary effusions. cardiac failure is common.

Generally, a solitary nodule to be appereciable by hand , should be at least 1 cm In diameter. The thyroid nodule always moves with deglutition unless it is adherent To a neighboring tissue by malignant process or rarely Reidel's thyroiditis. The lower border of the swelling if palpable suggests no retrosternal extension. The consistency of the nodule is deceptive. A cystic nodule may appear firm. A soft nodule does not rule out malignancy as follicular carcinoma may appear soft.

A hard nodule suggests malignancy, but can also be due to calcification in an adenomatous nodule. Cystic variety of papillary carcinoma is known to occur. Adenoma and cystic degeneration in an adenomatus nodule can present as cysts. Mobility of the nodule if restricted suggests malignancy.

Trachea may be deviated to opposite side by the pressure effect of nodule. Carotid artery may be pushed laterally by benign lesions and pulsation may be absent at the level of gland in cases of malignancy (**Berry' s sign).**

Regional lymph nodes i.e. pretracheal, paratrachal, lower deep cervical and sometimes upper deep cervical may be enlarged and palpable, due to metastases from papillary carcinoma of thyroid. Cystic degeneration may also occur in these lymph nodes.

Thus by clinical examination it is difficult to find out the aetiology of solitary nodule. It is impossible to make a diagnois of malignant nodule clinically unless certain features of malignancy are obvious such as:

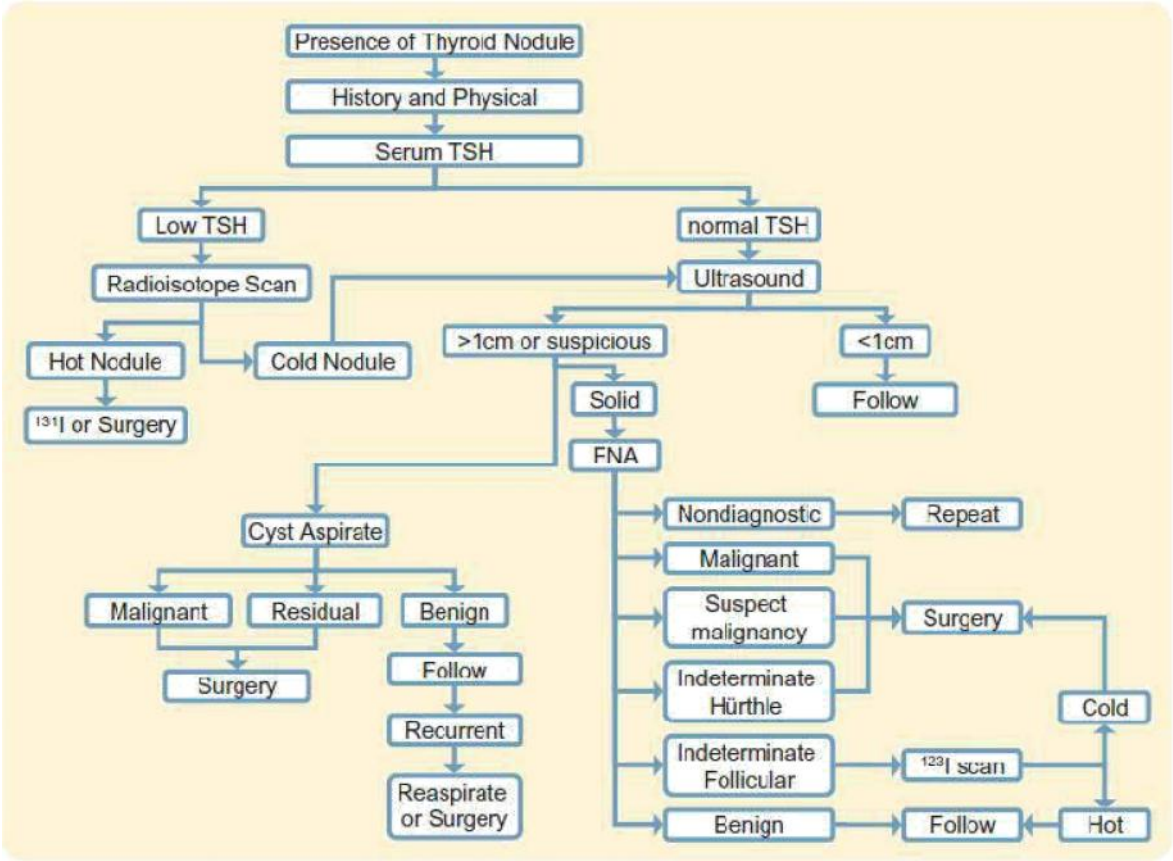
1. Hoarseness of voice
2. Cervical lymphadenopathy
3. Distant metastasis
4. Hard consistency

5. Fixity of nodule

6. Berry's sign

Absence of the features by no means rules out the possibility of malignancy, thus, making the solitary nodule clinically nodule clinically problematic.

WORK PLAN FOR SOLITARY NODULAR GOITRE



INVESTIGATIONS

ROUTINE INVESTIGATIONS:

As in other general surgical cases, routine investigations like blood analysis (Hb%, BT, CT), urine analysis, radiological assessment of chest are done to assess the fitness of the patient to undergo major surgical procedure.

SUPPORTIVE INVESTIGATIONS :

1) Sleeping pulse rate: To differentiate tachycardia due to anxiety from that of thvrotoxicosis, pulse rate is counted when the patient is asleep. A count of more than 90/min is suggestive of hyperthyroidism. A rate of 90-100/min indicates mild, 100-110/min moderate and more than 110/min severe hyperthyroidism.

2) ECG: In hypothyroid state, low voltage, flattened ST wave or inversion of T waves are seen. In hyperthyroidism sinus tachycardia, atrial tachycardia, atrial fibrillation and signs of left ventricular hypertrophy may be seen.

3) Serum cholesterol: In hypothyroidism, it is markedly increased (more than 300mg%).

4) Serum creatinine: Raised serum creatinine in presence of toxic features confirms thyrotoxicosis even though BMR is normal. In all, muscle wasting disorder should be ruled out.

5) Indirect laryngoscopy: Routine laryngoscopic examination should be made before thyroidectomy.3-5% of the patients have paresis or paralysis of one vocal cord probably due to exanthemata during childwood. Pre-operative detections of vocal cord paralysis protects the surgeon from possible litigation. It also helpful in diagnosing involvement of recurrent laryngeal nerve.

6) Radiological investigation:

Radiography of neck : It is helpful in determining the position of trachea, retrosternal extension and also calcification in the nodule. Calcification is seen in long standing adenomatous goiter and papillary carcinoma and extensive calcification in nodular goiter.

7) Basal metabolic rate (BMR): BMR measures oxygen consumption per minute. In hyperthyroid patients BMR will be raised. Non specificity of the test, lead to its almost disappearance from the scene in the diagnosis of hyperthyroidism.

8) SPECIFIC INVESTIGATIONS :

i) Tests for thyroid function :

Most of the patients with solitary thyroid nodule are euthyroid, but laboratory confirmation of this is generally agreed that no single procedure, consistently yields reliable basis for diagnosis and therefore, a combination of various tests are generally required.

Total thyroid hormones: The most useful index of thyroid function is the directmeasurement of circulating thyroid hormones. Total T4 and total T3 are designated T4 and T3 respectively. These are measured by radioimmune assays.

Normal values :

T4 : 55-155 nmol/lit.

T3 : 1-3 nmol/lit.

The commonest fallacy of estimation is, it measures total T4 and fails to detect thyroid binding globulin only. It is necessary to have information of binding protein to interpret T4 and T3 values. Factors that increase thyroxine binding globulin (TBG)

concentration (estrogens, pregnancy, liver disease) may elevate T4 and T3, decrease in globulin occurs. In nephriticsyndrome, Patients on androgens,glucocorticosteroids, hypoproteinemia, cirrhosis and acromegaly. In many centers, the use of T3 resin binding test is still as an indirect measurement of circulating thyroid hormone.

ii) Tests for thyroid binding proteins:

This test measures unoccupied thyroid hormone binding sites on TBG. This is done by using T3 resin uptake test (T3 RU). Radioactive T3 is inoculated with the patients serum, so that it becomes fixed to any thyroid binding protein not already carrying T3 or T4. The amount so fixed can be measured and from this can be estimated the number of binding sites in the serum which are un-occupied . In hyperthyrodism, the number of free binding sites of TBG is low because most of them are already carrying hormone, where as in hypothyroidism the number of free sites are high. Now -a-days using sephandex or thyopac method and taking 100% as the mean normal value for free binding sites, a figure of 85% or less suggest hyperthyroidism and a figure of 120% or more suggest hypothyroidism.

iii) Thyroid hormone indices (by calculation):

Free throxine (FTI)(FT4I) can be calculated as FTI = serum T4 **x** T3 uptake percent (T3RU). Similarly free T3 (Ft3I) can also be calculated. FT4I in euthyroid patients is 0.85 to 3.50 and that of FT3I is 1.4-3.7. It is probably the best parameter of thyroid function at the present moment.

iv) Free thyroid hormone measurements:

Ft4 can be measured by two methods: equilibrium dialysis or radio immunoassay (RIA). Dialysis methods is the gold standard, however, is restricted to research laboratories as it is time consuming and only a small number of samples can be processed. Simultaneously ft4 measurements by RIA is valuable and it provides an excellent index of

thyroid status in almost any clinical situations. Normal ft3 is 1.3-3.5 nmol/l and ft4 is 170-160 nmol/l (12-28 pmol/l).

v) Serum thyroid stimulating hormone (TSH):

Another very sensitive test of thyroid function is the serum TSH value. This is measured by immunoassay technique. The normal serum TSH level is 0.3-5miu/l. It is raised in primary hypothyroidism (may be over 40 miu/l) and almost undetectable in hypothyroidism. It is the most sensitive test of primary hypothyroidism.

vi) Tests of hypothalamic-pituitary axis of TRH test:

Thyrotropin releasing hormone (TRH) is produced in para-ventricular nucleus of hypothalamus and passes through the median eminence of anterior pituitary via the hypophyseal portal system. When TRH, a hypothalamic releasing factor is given intravenously in a dose of 200 pg to a normal individual, the level of TSH in the serum raises from the basal level of about 1µu/ml at 20 minutes and returns to normal by 120 minutes. This is a time consuming test and only occasionally gives information not obtained from routine tests of thyroid function.

vii) ***Radioiodne uptake (RAIU)test****:*

Routine isotope scanning has been abandoned except when toxicity is associated with nodularity.

viii) Thyroid scintigraphy : The use of radionuclide agents has been helpful in delineatingthe presence, size, and function of thyroid nodules. Two radioactive iodine isotopes have been employed, in clinical use, scanning with ^{123}I (dose of 1-2 Ci) has its advantage of low dose radiation (30 m rad) and short half- life (12-14 hours). This compares favourable with the use of ^{131}I (dose of 5 mCi) which has a higher dose of radiation (500 m

rad) and longer half-life (8 to 10 days). Scanning with ^{123}I is usually used for Patients with differentiated thyroid carcinoma to screen for distant metastasis. The best radionuclide is ^{123}I but now most of them are preferring 1-2 mCi of 99m Tc pertechnate (half-life 6 hours) given by IV injection and image after 5-10 min. ^{123}I is trapped and bound tothyroglobulin by the thyroid follicular cells, whereas 99m Tc is only trapped but not organified. Screening with 99m Tc also shows uptake in salivary glands and major vascular structures and therefore requires high sophistication of interpretation. 99Tc pertechnate is preferred for imaging agent when:

a. Patient is taking thyroid blocking agents

b. Patients is unable to take medication orally.

c. The study must be completed less than 2 hours

d. Thyroid function (uptake measurement) is not necessary.

Indication for thyroid scan :

1. Determine the size of thyroid
2. Depending on the ability to take up isotope than the surroundings, nodules are divided into:

   a . Hot nodule (hyperfunctioning) (5%). The incidence of malignancy is 4%.

   b. Warm or neutral nodule (10-15%). The incidence of malignancy in 9%.

   c. Cold nodule (hypo functioning) (80-85%). The incidence of malignancy is 15-20%.

3. Determining the retrosternal shadow on chest x-ray is a thyroid.

4. Differentiate between an autonomously functioning nodule from an hyperactive multi-nodular gland with a dominant nodule.

5. Post operatively to assess the residual thyroid tissue left behind after total thyroidectomy and whole body scintigraphy to detect secondaries from differentiated thyroid carcinoma.

Limitations of radionuclide scan :

1. It cannot differentiate benign from malignant nodule, other pathological conditions which produce cold nodule include adenoma, adenomatous hyperplasia, colloid cyst, haemorrhagic cyst, Hashimoto's thyroiditis, sub-acute thyroiditis and a large parathyroid adenoma or cyst

2. Inadequate visualization of the nodules at the periphery, isthmus and cold nodules surrounded by normal thyroid tissue . Nodules <1 cm are usually not visualized as radioactivity form normal gland passes through it. This can be overcome by oblique and /or lateral images.

3. Certain artifacts such as an asymmetric of a lobe or a tortuous carotid artery may distort a normal gland thus producing an abnormal scan.

Following high dose of ^{131}I administration, patients are hospitalized in isolation until the retained radioactivity is less than 15 mCi or the radiation exposure rate from the patient is less than 2.5 Mr/hr at l meter. Other radionuclides utilized are Gallium 205, 99mTc pentavalent dimercatposuccinate (DMSA).

ix) Ultrasonography : Ultrasound is a simple, rapid, relatively cheap and noninvasive method to study the structure of thyroid. High resolution ultrasonography (7.5 to 10 MHz) is sensitive in identifying impalpable nodules as small as 0.3 cm in diameter. USG is useful

in distinguishing between solid and cystic lesions, they are rarely malignancy and mixed solid- Cystic lesions has a 5% risk of malignant. Cysts seen in USG, those larger than 3cm are malignant in 14% of cases. Currently USG is used in obtaining the accurate measurement of size of the nodule in a patient who is put on suppressive therapy, and guide FNAC of complex cystic lesion nodule that is situated posteriorly and to access cervical lvmphadenopthy. Benign lesion nodule shows "hallow sign " on USG and features suggestive of malignancy include hyperchoic pattern in complete peripheral halo, irregular margins and microcalcifications.

x) Computerized tomography and magnetic resonance imaging :

There is no place for CT scanning and MRI in routine evaluation except to determine the extent of a large cervical or retrosternal thyroid and spinal metastases

xi) Tissue diagnosis :

a) fine needle aspiration cytology (FNAC):

The wide spread use of FNAC in diagnostic assessment has led to an increased incidence of malignancy with a concomitant reduction in cases requiring thyroid surgery producing a favorable cost reduction. FNAC is, therefore, a highly accurate and cost effective diagnostic technique of low morbidity providing a valuable to clinical assessment in overall selection of patients with thyroid nodules for surgery. The sensitivity of FNAC for detection of malignant lesions is approximately 83% and the specificity is about 92%. Problems with FNAC include difficulty in differentiating follicular adenoma from carcinoma.

Pit falls in FNAC of thyroid as mentioned by Shaha.

- adequacy of specimen (quantitative and qualitative).
- adequacy of specimen (no homogenicity of needle placement0.
- accuracy of cytopathologic interpretation.
- cysts (difficulties with degenarate nodules).
- Follicular lesions (benign Vs malignant).
- Hurthle cell lessions (benign Vs malignant).
- Lymphocytic lesions (lymphocytic thyroiditis Vs lymphoma)

b) Core needle biopsy :

This is done under local anaesthesia, is occasionally of value in establishing diagnosis in a patient with a patient with a large often hard and fixed mass in the neck frequently on the basis of anaplastic carcinoma or thyroid lymphoma. Core biopsy produces a small cylinder of tissue which is subjected to histopathological examination. Because of the caliber of the needle and the consequent haemorrhage, haematoma, injury of trachea and damage to RLN, there is no place for large needle biopsy of this type in the routine evaluation of solitary nodule thyroid.

xii) Serum Thyroglobulin (Tg) :

Normal levels 1-43 ng/ml. Tg may be elevated in patient with follicular or papillary carcinoma. However, its usefulness in preoperative evaluation lacks specificity, because Tg concentration is also elevated in thyroiditis, follicular adenoma, MNG. It is useful in post-operative period after total thyroidectomy for long term follow up in whom a marked rise may herald recurrence. It is especially helpful in cases where metastasis fail to concentrate RAI. Tg levels do not always correlate with extent of recurrence or metastatic disease. After total thyroidectomy during follow up if Tg>10 ng/ml, it indicates recurrences or metastasis.

xiii) Serum Calcitonin:

Calcitonin hormone secreted by para-follicular C-cells serves as useful marker in detection and follow up of medullary carcinoma. Elevated serum calcitonin in a patient with thyroid mass is virtually diagnostic of medullary carcinoma. Occasionally patient with these tumor and many with familial C-Cell hyperpasia have normal baseline level. They demonstrate rise in calcitonin concentration following provocative calcium infusion or pentagastrin stimulation

xiv) Measurement of antibobies :

About 95% of patients with Hashimoto's thyroiditis and 80% with Grave's disease have detectable anti-microsomal antibodies. Anti-microsomal antibodies are found in with Hashimoto's, Anti-TSH antibodies are detectable in patients with autoimmune hyperthyroidism (Grave's disease)

TREATMENT

The common indications for surgery in a solitary nodule are as follows :

1) Pressure effects, irrespective of aetiological diagnosis .

2) Malignancy.

3) Cosmesis .

The treatment for different aetiological entities can summarized as follows:

1] **Adenomatous non–toxic nodules**

As the basic cause is diminished synthesis of thyroxine in the body the entity should be treated by thyroxine replacement therapy (0.1- 0.2 mg /day) preferably

serum levels of T3, T4 and TSH be measured at regular intervals and level should be monitored by adjusting the dose of oral thyroxine administration some nodules regress during therapy. if the nodule is large causing pressure effects or if it is cosmetically not acceptable to the patient surgery is indicated hemithyroidectomy is done. All these should be followed up post operatively and thyroxine replacement therapy should be instituted to prevent recurrence

2] **Lymphocytic thyroiditis :**

It eventually result in hypothyropidsm, treatment is essentially conservative consisting of careful follow up; oral thyroxine substitution therapy by monitoring the serum levels of T3, T4, TSH. There is no scope for surgery except for pressure effects by a large nodule or for cosmesis

3) Toxic nodule:

It is an autonomously functioning thyroid nodule that produces hyperthyroidism. Toxic nodule can be treated by surgery or radioactive iodine therapy. Radioiodine is the treatment of choice over the age of 45 years, as toxic nodules are rarely malignant, provided all the following criteria are satisfied.

- patient should have completed family (either postmenopausal or sterilized).
- There should be no pressure effects
- Cosmetically, these nodules should be acceptable as the size of the nodule may not regress with radioiodine.

If any of the above mentioned criteria is not satisfied, surgery is indicated. Treament is by hemithyroidectomy since the rest of the gland is suppressed by toxic nodule, post -operative hypothyrodism rarely occurs.

4) Thyroid cyst :

About 15% of all thyroid nodules are cystic. Majority of them (97%) are benign. Very rarely, papillary carcinoma can present as cyst due to degeneration.

All thyroid cysts initially treated by simple aspiration by a needle and centrifuged Aspirate sent for cytopathology. After aspiration, the thyroid is palpated and if There is any solid remnant, aspiration, aspiration biopsy of cyst wall is done to Rule out malignancy. Simple thyroid cysts resolve with aspiration in approximately 75% of cases, although some require second or third aspiration. If the cyst persists after 3 Attempts at aspiration, surgery is recommended. Surgery is also recommended for cysts greater than 4 cm in diameter and for complex cyst with sold and cystic components, because the latter have a higher incidence of malignancy (15%)

5) Benign neoplasms:

In the light of our present knowledge it is extremely difficult to separate benign adenoma.A limited resection in the form of hemithyroidectomy is done. Further treatment depends on histopathological examination. Should the report be a benign neoplasm no more treatment is required. Should it be malignancy, it shall be treated as discussed below

6) Treatment of papillary and follicular carcinoma:

The primary treatment for papillary carcinoma is surgical excision. The extent of resection, indication for regional lymph node dissection and post-operative follow up of patients are the most controversial aspects of management. Because of slow growth of these well differentiated neoplasms and the overall good prognosis, recurrence of CA occur several years after surgeryThe various treatment options are discussed as follows:

A) Surgery (Total thyroidectomy/Near total thyroidectomy):

The procedure involves removal of the entire thyroid gland with identification and preservation of recurrent laryngeal nerves and parathyroid glands. Reasons for total thyroidectomy.

1. Enables one to use RAI effectively to detect and treat thyroid tissue or metastatic disease.
2. Makes the serum TG level more sensitive maker of recurrent or persistent disease.
3. Eliminates the contralateral occult cancers as sites of recurrence (because up to 85% of tumors are multifocal).
4. Reduces the risk of recurrence and improves survival.
5. Decrease the 1 % risk of progression to undifferentiated or anaplastic thyroid cancer.

6. Reduces the need for re-operative surgery with its attended risk of increased complication rates.

Post-operative management:

Adjuvant therapy :

i) Suppressive therapy with thyroxine:

Post-operative thyroid hormone replacement is necessary after total or near total thyroidectomy or ablation with radio-iodine. Thyroxine is necessary not only as replacements therapy in patients total thyroidectomy but has additional effect of suppressing TSH and reducing growth stimulus for any possible residual thyroid cells. TSH suppression reduces tumor recurrence rates particularly in young patients with thyroid cancer.

Oral Levothyroxine is begun before discharge at an average dose of 100 micro gm/day. Adequacy of thyroid hormone replacement is assessed by measuring T4 and TSH at 6 to 12 weeks after surgery. The degree to which one suppresses TSH is a point of debate. It is advisable to keep the TSH at or below the normal range (0.5 to 5.0 microU/mL) in patients who are thought to be without evidence of disease and to maintain a lower TSH level (0.1 microU/mL) in patients with residual neck disease, metastases, or recurrent disease.

ii. Use of RAI post-operatively:

All patients who have undergone a total or near-total thyroidectomy for a papillary or follicular carcinoma larger than 1.0 to 1.5 cm should be considered candidates for radio-iodine ablation. ^{131}I ablation of any residual normal thyroid is important after what is thought to be complete resection of the primary tumor to aid in the detection of metastatic disease and to eradicate residual microscopic cancer.

The dose of ^{131}I for ablation is not standardized. Some recommend low dose ablation with less than 30 mCi given on an outpatient basis. This approach should be reserved for

low-risk young patients.Higher ablative doses ranging from 100 to 150 mCi should be used for older, high-risk patients, particularly those known to have an incomplete resection of the primary tumor, an invasive primary tumor, or metastases.

iii. Chemotherapy

The most effective non-surgical treatment for well-differentiated thyroid cancer is ablation with radio-iodine.

Progonosis :

Most patients with papillary carcinoma can be expected an excellent prognosis, with the 10-years survival rate approaching 95% for the most favorable stages.

Prognostic risk classification for patients with well – Differentiated thyroid cancer (AMES or AGES)

	Low risk	High risk
Age	< 40 years	>40 years
Sex	Female	Male
Extent	No local extension, intrathyroidal no capsular invasion	capsular invasion extrathyroidal extension
Metastasis	None	Regional or distant
Size	<2cm	>4cm
Grade	Well differentiated	Poorly differentiated

AGES - age, pathology of tumor, extent and size of the primary tumor; AMES-age, distant metastasis, extent of the primary tumor, and size of the primary tumor.

MATERIALS AND METHODS

The present study on “Clinical Study of the incidence of malignant changes in Solitary Nodule of Thyroid” has been conducted by utilizing cases admitted and managed in the Department of Surgery at thirunelveli medical college

Prospective analysis of 50 cases of solitary nodule thyroid in the specified period done. These cases were selected by random sampling method and studied in detail clinically and recorded as per the proforma. Routine investigations and specific investigations including FNAC of the nodule, Thyroid profile, IDL, Plain X-ray neck, USG neck were done in all cases. Special investigations like radio-isotope scanning was not performed as the facilities were not available. All the patients were managed by surgery and diagnosis was confirmed by histo-pathological examination.

The patients were grouped according to different variables like age , sex, size of the nodule, site of the nodule, functional thyroid status, FNAC reports and histo-pathological examination reports, then analyzed and compared with the previous similar studies conducted elsewhere. Finally conclusions were drawn accordingly.

Treatment :

Pre-operative :

Use of anti-thyroid drugs, beta-blockers, blood transfusions or any other medications were prescribed based on individual status and was noted

Operative:

Position of the patient, type of anaesthesia, incision, type of operation planned, per-operative findings and type of operation performed were recorded.

Post-operative:

Every patient was followed up post-operatively during the course of management in the hospital to note the development of and management of complications.

Follow-up:

At the time of discharge, all the patients were advised to attend the surgical OPD regularly for follow up. Any recurrences or complications were noted. Thyroid functional status was assessed, accordingly thyroxine tablets prescribed if necessary.

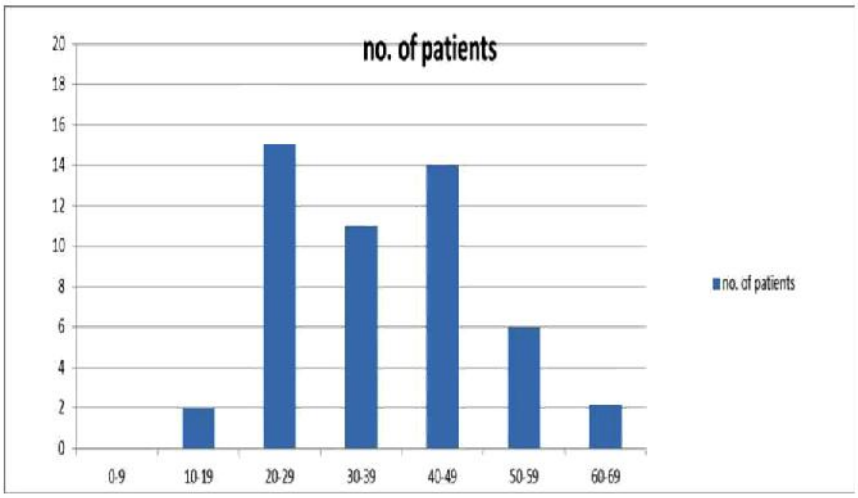
RESULTS

Total of 50 cases of solitary nodule of thyroid studied and following conclusions were drawn:

Age Incidence:

The age of the patients ranges from 18 years to 66 years, with peaks being in 3^{rd} to 5^{th} decades. The mean age of presentation is 37.24 years. Cases in 3^{rd} to 5^{th} decades constitutes 60% of the cases studied.

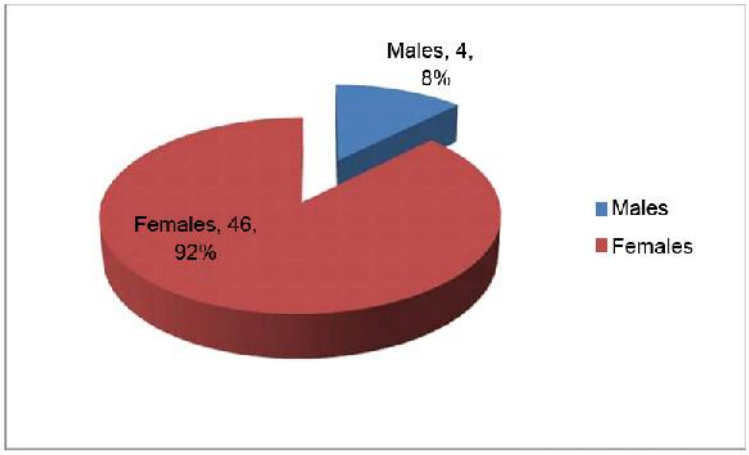
AGE IN YEARS	NO. OF PATIENTS
0-9	0
10-19	2
20-29	15
30-39	11
40-49	14
50-59	6
60-69	2
TOTAL	50



Sex Incidence:

Solitary nodule of thyroid are much more common in females. Out of 50 cases studied 46 were females and 4 were males, and the ratio comes to M : F = 1 : 11.5 . Also the malignant nodules are common in females. Out of 6 cases of malignancy in the study, 5 were females.

Sex	no. of patients
Males	4
Females	46
Totals	50



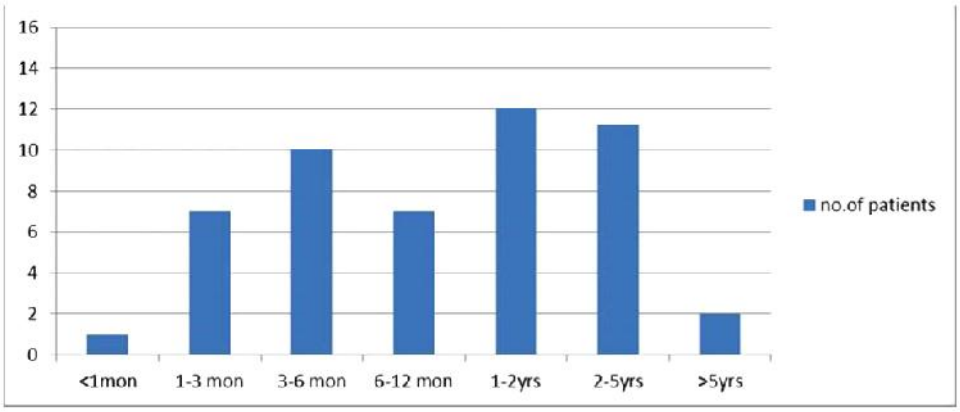
Clinical features:

All the cases in the present study presented complaint of swelling in the region of the thyroid. Only few patients presented with pain, discomfort and dysphagia. All the mentioned additional symptoms were of mild degree. Out of 50 cases, 3 cases had pain, 3 cases had discomfort and another 2 had dysphagia. Also none of the patient had lymphadenopathy which was confirmed by ultrasonographic examination. Two patients had symptoms of thyrotoxicosis, and one had features of hypothyroidism. The latter patients' thyroid profile confirmed the functional status.

Duration of symptoms:

In our study, duration of onset symptoms varied from 15 days to 8 years. Also duration of malignant nodules extend from 1 month to 4 years.

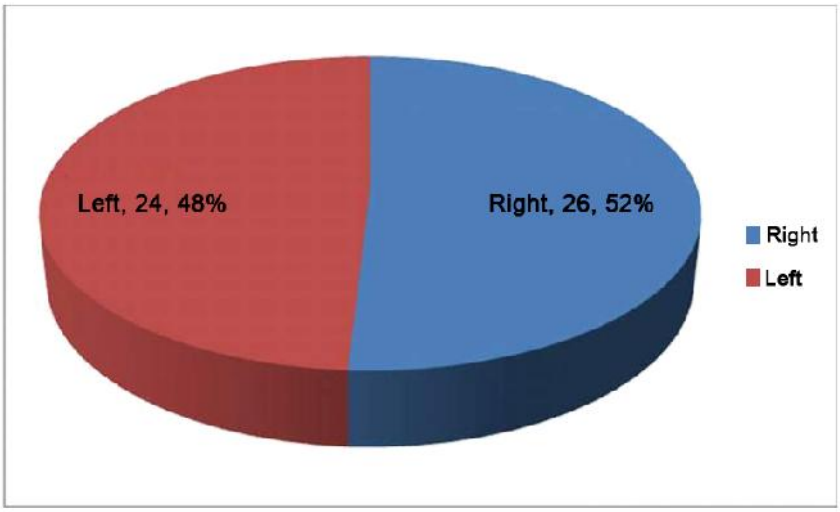
Duration of Symptoms	no.of patients
<1mon	1
1-3 mon	7
3-6 mon	10
6-12 mon	7
1-2yrs	12
2-5yrs	11
>5yrs	2



Site of the nodule:

Out of 50 cases studied, 26 cases presented with nodule in right lobe of the thyroid gland and the remainder in the left lobe of thyroid. One patient among left sided solitary nodule had undergone right lobectomy 30 years back and presented with recurrent nodule in the rest of the lobe.

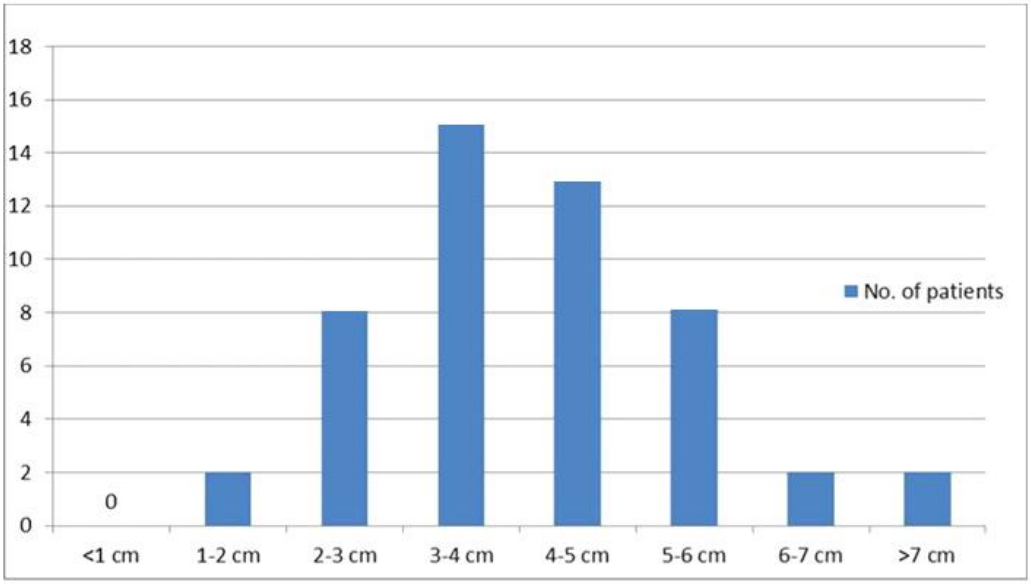
site of the nodule	no. of patients
Right	26
Left	24
Total	50



Size of the nodule:

In the present study, on clinical examination size of the nodule, in its largest dimension, varies from 2cm to 12cm. Most of the patients presented with the size of about 3 to 5 cm. in the study, as such there is no correlation between the size of the nodule and the occurrence malignant nodule.

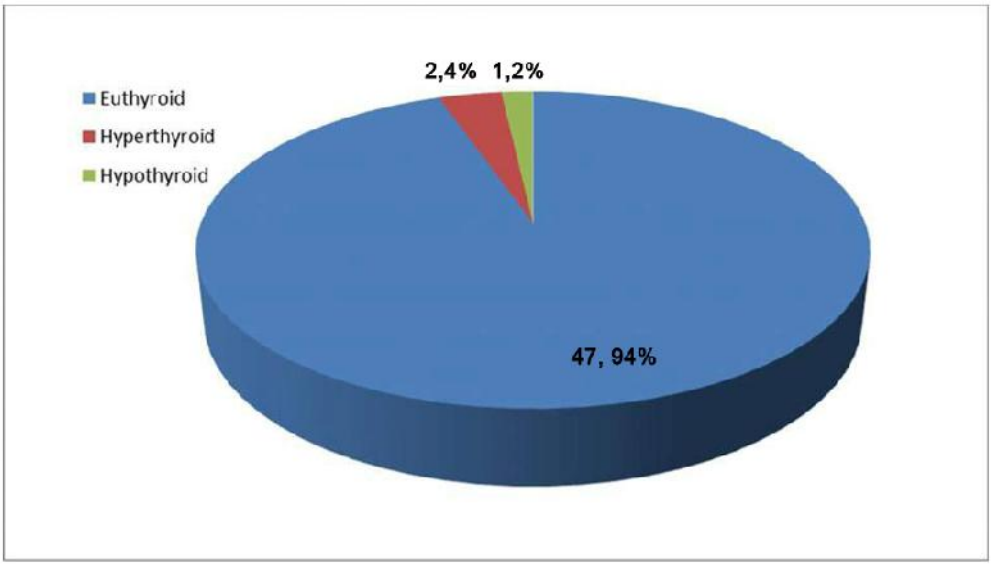
Size of the Nodule	No. of patients
<1 cm	0
1-2 cm	2
2-3 cm	8
3-4 cm	15
4-5 cm	13
5-6 cm	8
6-7 cm	2
>7 cm	2



Thyroid functional status:

Out of 50 cases, two presented with features of thyrotoxicosis, one with hypothyroidism and rest all were in euthyroid state. Patients with thyrotoxicosis were made euthyroid using antithyroid drugs and operated and both cases turned out to be toxi follicular adenoma. Patient with hypothyroidism was treated with thyroxine, USG neck revealed multiple nodules and managed by subtotal thyroidectomy, histopathological examination confirmed the diagnosis of multi-nodular goiter.

thyroid functional status	No. of patients
Euthyroid	47
Hyperthyroid	2
Hypothyroid	1
Total	50

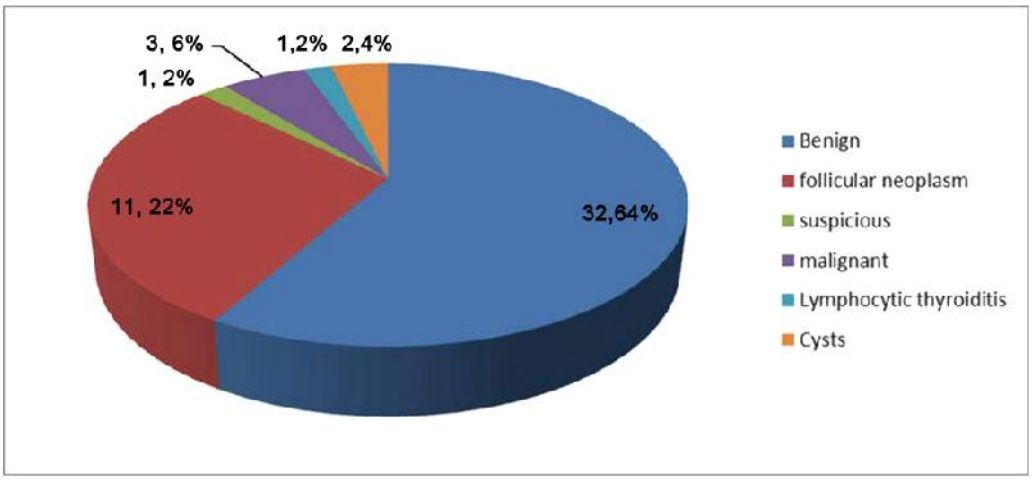


FNAC Reports:

Fine Needle Aspiration Cytology is the important investigation in the evaluation of solitary nodule of thyroid. All 50 cases were subjected to FNAC during the course of evaluation. Fnac reports are mainly categorized into 6 entities- Benign, follicular neoplasm, suspicious(of malignancy), malignant, lymphocytic thyroiditis, cysts. In our study, out of 11 follicular neoplasms, two turned out to be follicular carcinoma. One suspicious (of papillary carcinoma) case confirmed papillary carcinoma on histopathological examination. Three cases of papillary carcinoma were diagnosed pre-operatively by FNAC alone.

Two cases diagnosed as cysts by FNAC confirmed to be simple cysts on histopathological examination.

FNAC reports	No. of patients
Benign	32
Follicular Neoplasm	11
Suspicious	1
Malignant	3
Lymphocytic Thyroiditis	1
Cysts	2
Total	50



Aetiological incidence of solitary nodule of thyroid:

Out of 50 cases studied, common causes of solitary nodule are MNG, follicular adenoma and adenomatous goiter; the most common being MNG which constitutes about 36% of cases.

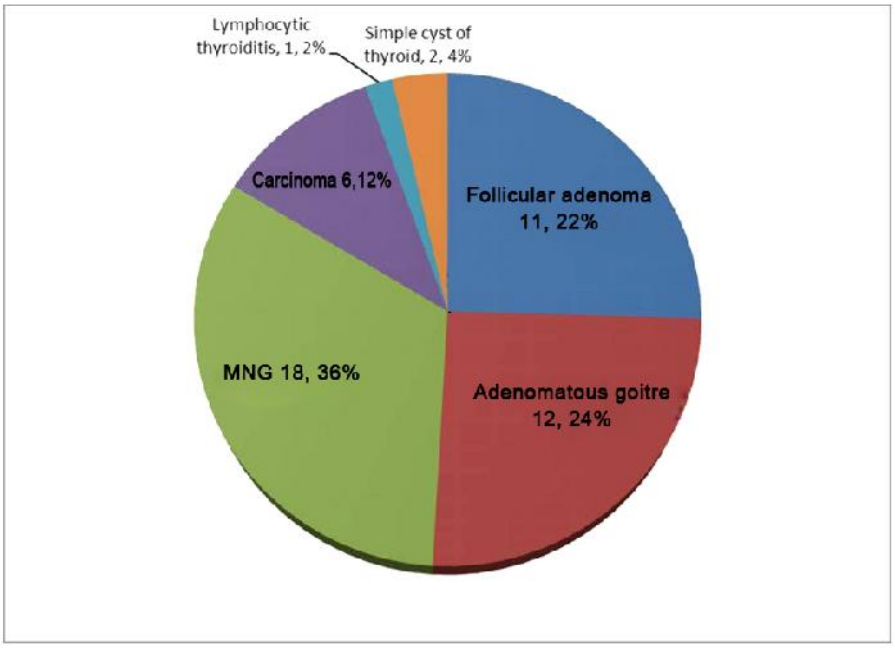
Follicular adenomas have 22% and adenomatous goiters have 24% incidences.

Out of 50 cases, six were malignant – 4 papillary carcinoma and 2 follicular carcinoma.Ultrasonography detected suspicious findings in two cases among six malignant cases – 1 papillary and 1 follicular.

Three cases of papillary carcinoma were diagnosed with certainity by FNAC, one case was suspicious which turned out to be papillary CA on histopathological examination.

Two cases of follicular carcinoma were diagnosed follicular neoplasm, one of them showed suspicious features on ultrasonographic examination.

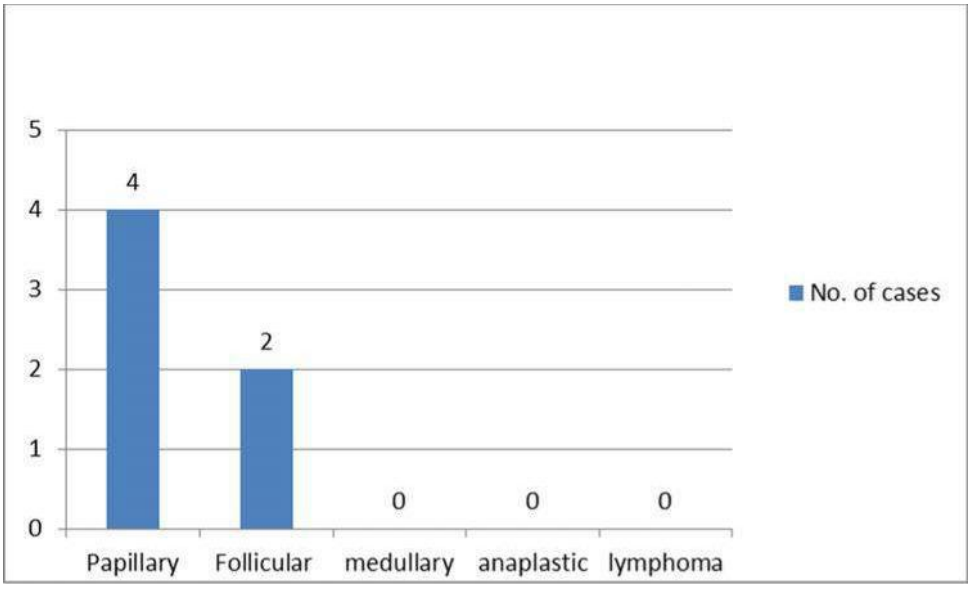
HPE Reports	No. of patients
Follicular adenoma	11
Adenomatous Goitre	12
MNG	18
Carcinoma	6
Lymphocytic thyroiditis	1
Simple cyst of Thyroid	2
Total	50



Type of carcinoma:

From the study, out of 6 carcinoma, 4 were papillary and 2 follicular: no case of medullary or anaplastic or lymphoma was detected. Papillary carcinoma accounts to 67% and follicular carcinoma accounts to 33%.

carcinoma	No of cases	percentage
Papillary	4	67
Follicular	2	33
medullary	0	0
anaplastic	0	0
lymphoma	0	0
Total	6	100



SURGERY / OPERATIVE PROCEDURE DONE:

Depending upon the clinical diagnosis and FNAC features, all the 50 patients undergone surgery. Among them, 31 patients had undergone hemithyroidectomy, 12 cases undergone sub-total thyroidectomy and 7 cases undergone total thyroidectomy.

In one case, HPE after hemithyroidectomy showed follicular carcinoma, then completion of total thyroidectomy done. In another case with recurrent nodule (previously hemithyroidectomy was done 30 yrs back), total thyroidectomy was done, which showed features of MNG.

Post-operatively, suppressive dose of thyroxine was started for patients who had undergone total thyroidectomy. Three cases out of 7 cases of total thyroidectomy showed features of hypocalcemia on 2-4 post-operative day, hence, they are supplemented with oral calcium and vitamin D3.

All the cases were followed up for 6months, two cases had husky voice without any change in vocal cord movements.

DISCUSSION

The observations and results of the present study were compared with the available previous similar studies.

MEAN AGE AT PRESENTATION:

AUTHORS	MEAN AGE IN YEARS
Das DK (1999)	35
Talepoor M(2005)	38.6
Quari F. (2005)	36.7
REHMAN A.U.(2009)*	34.7
Khurshid Anwar(2012)*	37
Present study	**37.24**

In the study done by Quari F and Talepoor M separately in 2005, reported the mean age at presentation as 36.7years and 38.6years respectively. Khurshid Anwar reported, in 2012, the mean age of presentation as 37years. From the present study, the mean age at presentation found to be 37.27years, correlates with the previous studies.

Most of the earlier series reported peak incidence of solitary nodule thyroid in the 3^{rd} and 4^{th} decades. Bhansali S.K [5](1982), in his similar study , reported the peak incidence in 4^{th} and 5^{th} decade. In the present study, the peak incidence found to be 3^{rd} to 5^{th} decades, which constitutes about 60% of the cases studied.

SEX DISTRIBUTION:

AUTHOURS	**SEX INCIDENCE(M:F)**
Dorairajan (1996)	1:9
Das DK(1999)	1:5.39
Gupta C(2001)	1:5
Present study	**1:11.5**

In the study done by Dorairajan(1996) and Das DK(1999) reported ratio of sex incidence as 1:9 and 1:5.39 respectively. In the present study, its found to be 1:11.5, which correlates with previous studies.

Because of periods of fluctuations in the demands of the hormonal requirement in female in their life cycle(puberty, menstrual cycles, pregnancy, menopause), the chances of thyroid nodule formation are very high as compared with male counterparts.

Distribution of non-neoplastic and neoplastic lesions diagnosed by FNAC:

AUTHOURS	**NON-NEOPLASTIC**	**NEOPLASTIC**	**RATIO**
Sarda AK(1997)	487	59	8.25:1
Das DK(1999)	346	85	4.07:1
Gupta C(2001)	470	30	15.66
Karur(2002)	32	15	2.13:1
Talepoor M(2005)	325	70	4.33:1
Hurtado Lopez M(2005)	80	50	1.6:1
Nagada(2006)	51	18	2.83:1
Chao CT(2007)	276	264	1.04:1
Present study	**36**	**14**	**2.57:1**

In the present study, neoplastic conditions include adenomas and all malignant lesions. From the study, the ratio of non-neoplastic to neoplastic cases is about 2.57:1, which is comparable to the studies done earlier like Karur(2002), Hurtado Lopez M(2005), Nagada(2006), Chao CT(2007).

Distribution of malignancies by FNAC :

AUTHOURS	**PERCENTAGE**
Sarda Ak et al(1997)	10.8
Karur K et al(2002)	18
Mundsad B et al(2006)	4.16
Present study	**7.27**

In the present study, among 4 cases of papillary CA, 3 were diagnosed with certainty by FNAC and the rest one was suspicious of malignancy. But both the follicular CA were initially reported as follicular neoplasm. From the study, distribution of malignancy is about 7.27, which is comparable with the earlier studies.

Aetiological incidence (in percentage):

Series	MNG	ADENOMA FOLLICULAR	CARCINOMA	OTHERS	Total No. Of cases
Zaman & Bhagbati(1971)	83	9	8	-	2221
Ananth Krishnan (1983)	12	47	2	2	104
Bhansali(1982)	71	20	9	-	449
Fenn(1980)	22	55	12	11	342
Kapur(1982)	28	50	11	11	221
Present series	**36**	**22**	**12**	**30**	**50**

From the present study, commonest cause of solitary nodule is MNG, which is comparable with the studies done by Fenn(1980) ,Kapur (1982) ,Bhansali(1982). The common causes are follicular adnoma and adenomatous goitre.

Incidence of carcinoma:

STUDY	YEAR	PERCENTAGE
A S Fenn et al	1980	12.0%
Bhansali S K	1982	9.0%
Kapur et al	1982	11.0%
Wagana et al	2002	16%
Rehman A U	2009	11.4%
Present study	**2015**	**12.0%**

From the literature, the incidence of malignancy in thyroid nodule ranges from 5% to 30%. From the present study, the incidence found to be 12 %, which is comparable with the study done by A S Fenn et al, Kapur et al, Rehman A U.

CONCLUSIONS

The present study is a prospective analysis of 50 cases of solitary nodule of thyroid, admitted in Thirunelveli medical college. Though a large number of patients are required to come to better conclusions, based on the data and results obtained in the present study, the following conclusions can be drawn:

- Solitary nodule of thyroid is more common in females.
- Solitary nodule of thyroid is more common the age group of 20-50years.
- Most of the patients with solitary nodule of thyroid present with swelling alone.
- Most of the patients with solitary nodule of thyroid are in euthyroid state and only few present with toxicity and hypothyroidism.
- Incidence of malignancy in male patients presenting with solitary nodule thyroid is more when compared to female patients presenting with the same.
- commonest cause of solitary nodule of thyroid is multi-nodular goitre.
- USG can be used to detect multi-nodular goitre in patients presenting with solitary nodule thyroid.
- FNAC is the investigation of choice in the evaluation of solitary nodule of thyroid. It has few pitfalls. In such situations, only histopathology can confirm the exact pathology. It detects papillary carcinoma in a solitary nodule with high sensitivity and specificity.
- Papillary carcinoma is the most common malignancy of thyroid, followed by follicular carcinoma.

SUMMARY

A prospective analysis of 50 cases of solitary nodule of thyroid, admitted inthirunelveli medical college has been made and summarized below:

- Commonest presentation of solitary nodule is swelling in front of neck.
- The peak age at presentation of solitary nodule thyroid is 3rd to 5th decade, constituting about 60% of the cases.
- Solitary nodule is more common in females with the ratio M:F = 1:11.5.
- Most of the solitary nodule of thyroid are benign (88%).
- Most of patients with solitary nodule of thyroid are in euthyroid state(94%).
- After evaluation of solitary nodule thyroid,36% of all the clinically solitary nodule turned out to be multi-nodular goitre.
- Common causes of solitary nodule thyroid are MNG (36%), follicular adenoma(22%) and adenomatous goitre(24%).
- Incidence of malignancy of solitary nodule is about 12%. Male to female ratio in case of malignant nodule is 1:5.
- Incidence of carcinoma in males presenting as thyroid nodule is higher (25%) compared to that of females (10.87%).
- The most common malignancy in solitary nodule thyroid is papillary carcinoma (67%), followed by follicular carcinoma(33%)
- FNAC is an important investigation in the evaluation of the solitary nodule of thyroid.
- Surgery has been the treatment of choice in most of the cases, either because of cosmetic reasons or toxicity or FNAC diagnosis of follicular neoplasm or malignancy.
- Transient hypocalcemia is common after total thyroidectomy for malignancies.

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ANNEXURE-1

PROFORMA FOR CLINICAL STUDY OF SOLITARY NODULE OF THYROID

Case No:

Name: Hospital:

Age: Unit:

Sex: D.O.A:

Occupation: D.O.D:

Address:

Contact No:

A. **Clinical diagnosis**:

B. Chief complaint and its duration:

a. Swelling

b. Pain

c. Others

C. History of presenting illness:

a. Swelling

i. Duration

ii. Site

iii. Mode of onset

iv. Progress of the swelling

v. Presence of other swelling(s)

vi. Secondary changes

b. Pain

i. Duration

ii. Onset

iii. site

iv. Nature

v. Radiation

vi. Aggravating factors

vii. Relieving factors

c. Pressure symptoms

i. Dysphagia

ii. Dyspnea

iii. Hoarseness of voice

iv. Voice fatigue

d. Symptoms suggestive of BMR changes

i. Appetite: increased/decreased/good

ii. Weight: increased/decreased/no significant change

iii. Sweating: increased/decreased/no significant change

iv. Any preference to hot or cold environment

e. Toxic symptoms

i. Primary toxicity

1. Irritability
2. Insomnia
3. Anxiety
4. Fear
5. Tremors of hands
6. Prominence of eyes
7. Diarrhea
8. Swelling of lower limbs- pretibial myxoedema

ii. Secondary toxicity

1. Palpitation
2. Precordial pain
3. Dyspnea on exertion
4. Swelling of lower limbs

f. Hypothyroid symptoms

i. Dullness

ii. Lethargy

iii. Loss of hairs

iv. Behavior-hypoactivity

v. Response to surroundings

g. Menstrual history-menorrhagia/oligimenorrhoea/amenorrhoea

i. Flow

ii. Days

iii. Frequency

h. Symptoms suggestive of malignancy

i. Rapid increase in size

ii. Presence of other swelling(s) in neck – lymph nodes

iii. Recent onset of pressure symptoms/change in voice

iv. Chest symptoms- cough/breathlessness/hemoptysis

v. Loss of weight and loss of appetite

D. Past history:

i. h/o any drug intake

ii. h/o irradiation to neck in childhood

iii. h/o diabetes/hypertension/tuberculosis/asthma/allergy

E. Family history

iv. h/o similar complaints in family members

v. h/o similar complaints in locality

F. Personal history

vi. Diet:

vii. Appetite:

viii. Sleep

ix. Bowel and bladder habits:

x. Habits:

GENERAL PHYSICAL EXAMINATION

Appearance:

Look: Anxious/dull/normal

Built: thin/moderate/obese

Skin:

Hands: warm/moist/cold

Nutrition:

Tremors:

Vitals: pulse – rate:

- rhythm:
- volume:
- character:

Respiratory rate:

Temperature:

BP.:

Pallor:

Icterus:

Cyanosis:

Clubbing:

Lymphadenopathy:

LOCAL EXAMINATION

1. Inspection

Swelling(s)
- number:
- shape:
- size:
- borders:
- extent:
- surface:

- skin over the swelling:
- secondary changes: fungation/ulceration/inflammation -pulsation:
- engorged

veins: - trachea:

- any other swelling(s)-lymph nodes

2. Palpation:

-Local rise of temperature: -Tenderness:

- Number:
- Shape:
- Size:
- Site:
- Extent:
- Borders
- Surface:
- Consistency:
- Mobility -skin fixity
    - on contraction of muscle
    - anatomical plane
- Position of trachea:
- Carotids: normal/Displaced/Absent -Bruit:
- Dilated veins: -Regional lymph nodes:

3. Percussion:

- over sternum: Dull/Resonant

4. Auscultation:

- Tracheal position -Bruit

5. Measurement of neck at the most prominent part:

SYSTEMIC EXAMINATION

Signs of toxicity-Primary

-Secondary

1. Cardiovascular system:

2. Respiratory system:

3. Central nervous system:

4. Per-abdominal examination:

CLINICAL DIAGNOSIS:

INVESTIGATIONS:

ROUTINE:

HB%:	Total Count:
Differential Count:	ESR:
Bleeding Time:	Clotting Time:
Urine Routine: Albumin-	ECG:
Sugar & microscopy-	
Random Blood Sugar:	Blood Urea:
Serum Creatinine:	Chest-X-Ray:
HIV -1&2:	HBsAg:

SPECIFIC INVESTIGATIONS:

- FNAC of nodule:
- Thyroid Profile:
- Indirect Laryngoscopy:
- Plain X-Ray Neck:
- USG Neck:

TREATMENT:

Pre-operative:

Surgical:

- Operative Findings:

Post-operative:

HISTO-PATHOLOGICAL EXAMINATION: - Macroscopic:

- Microscopic:

FOLLOW-UP:

ANNEXURE-2

CONSENT FORM

I/We _____age_____Hosp. No. _____Ward _____, in my/our full senses hereby give my/our complete consent for _____ or any other procedure deemed fit which is a diagnostic / therapeutic procedure / biopsy / transfusion / operation to be performed on me / my son / daughter under any anesthesia deemed fit. The nature and risks involved in the procedure have been explained to me in my own language to my satisfaction. For academic and scientific purpose, the operation/ procedure may be recorded or photographed, or used for statistical measurements.

Signature/thumb impression

Of the patient/guardian

Date:

Place:

Guardian:

Relationship:

Full address

MASTER CHART

Serial No.	I.P. No.	Name	Age (Years)	Sex	Duration of	Pressure symptom	Toxic sym	site	Size (in cm)	Consistency	Lymph node(s)	Thyroid profile	USG	FNAC	surgery	HPE	
1.	1440	Rasitha banu	27	F	6mon	-		L	4*3	Firm	-	-	SN	FN	HT	FA	
2	2067	Nirmala	45	F	2y	Discomfort		R	6*4	Firm	-	Hypo	MN	NCG	NTT	MNG	
3	2717	maheswari	41	F	1y	-		R	7*4	Cystic	-	-	SC	CC SC	HT	SCT	
4	2727	Chithra	22	F	6mon	-		L	3*4	Firm	-	-	SN	NCG	HT	AT	
5	2926	monika	18	F	6mon	-		R	3*4	Hard	-	-	SN	PC	TT	Follicular var. PC	
6	3385	Pushpa	40	F	3mon	-		R	3*2	Firm	-	-	SN	FN	NTT	MNG	
7	4693	Saroja	62	F	2mon	-		L	5*4	Cystic	-	-	SN	CG SC	HT	SCT	
8	7180	Chandra	45	F	2y	-		R	5*6	Firm	-	-	MN	CG	STT	MNG	
9	7557	Annal	40	F	8mon	-		L	4*3	Firm	-	-	SN	FN	HT	FA	
10	7575	Saral beevi	30	F	1.5y	-		L	4*4	Firm	-	-	SN	FN	HT	FA	
11	8131	karupaiah	58	M	3mon	-		L	5*6	Firm	-	-	SN	CG	TT	MNG	
12	8779	Iyyammal	22	F	1mon	Discomfort		R	8*4	Firm	-	-	MN	CG	TT	MNG	
13	9443	Savitha	28	F	5mon	-	+	L	3*4	Firm	-	hyper	SN	FN	HT	FA	
14	9445	Ambujam	47	F	2y	-		R	6*4	Firm	-	-	SN	CG	HT	AG	
15	10882	Sumithra	47	F	4mon	-		L	4*3	Cystic	-	-	SN	CG	HT	AG	
16	11519	Savitha	25	F	1y	-		R	3*3	Firm	-	-	SN	FN	HT	AG	
17	11543	Gayathri	32	F	1y	-		R	5*4	Firm	-	-	SN	CG	HT	MNG	
18	12964	Manjula	25	F	1y	-		L	4*3	Firm	-	-	MN	NCG	STT	MNG	
19	13131	Vijaya	59	F	4mon	-		R	3*4	Firm	-	-	MN	NCG	STT	MNG	
20	14060	Lakshmi	30	F	1y	-		L	5*6	Firm	-	-	SN	CG	HT	AG	
21	14286	Vasanthi	51	F	2y	-		L	5*5	Firm	-	-	SN	NCG	HT	AG	
22	15511	Selvi	25	F	8y	-		R	4*5	Firm	-	-	MN	NCG	STT	MNG	
23	16150	Sundhari	58	F	3mon	-		L	2*2	Firm	-	-	MN	NCG	STT	MNG	
24	16214	Sangitha	62	F	1mon	pain		L	6*3	Cystic	-	-	SN	CC	HT	AG	

25	19844	rekha	22	F	1y	-		R	4*5	Firm	-	-	SN	CG	HT	FA	
26	22241	chithra	23	F	7mon	-		R	4*5	Firm	-	-	MN	NCG	STT	MNG	
27	22605	chanthra	40	F	2y	-		R	4*3	Firm	-	-	MN	NCG	STT	MNG	
28	22660	muthurani	50	F	2y	-	+	L	3*3	Firm	-	-	SN	FN	HT	FA	
29	23284	ulagammal	30	F	6mon	-		R	4*5	Firm	-	-	MNG	CG	STT	MNG	
30	23354	selvakumari	38	F	3mon	-		R	3*4	Firm	-	-	MN	NCG	STT	MNG	
31	27684	Manjula	24	F	4y	Dysphagia	no	R	12*10	Firm	-	-	SN	FN	HT	FA	
32	28960	sathya	36	F	2y	pain	no	R	7*6	Firm	-	-	SN	CG	HT	AG	
33	29193	Savitha	45	F	1y	-		L	4*4	Firm	-	-	SN	CG	HT	AG	
34	29597	meena	39	F	4y	-	no	L	5*5	Hard	-	-	[illegible]	PC	TT	PC	
35	1964	Saraswathi	21	F	1mon	-		L	2*3	Firm	-	-	SN	Susp PC	TT	PC	
36	3267	Nagoor meeral	40	F	2mon	-		R	3*3	Firm	-	-	SN	FN	[illegible]	FC	
37	6489	vaundaman	32	M	10mon	Dysphagia		R	5*4	Firm	-	-	SN	NCG	HT	FA	
38	6722	Manimegali	31	F	5mon	-		L	3*3	Firm	-	-	SN	FN	HT	FA	
39	6740	Jayasheela	19	F	4y	Mild discomfort		L	6*6	Firm	-	-	MN	NCG	STT	MNG	
40	11169	Ashwini	29	F	2y	-		R	4*5	Firm	-	-	SN	CG	HT	FA	
41	12339	Savitha	26	F	1y	-		L	4*3	Firm	-	-	MN	CG	STT	MNG	
42	13435	Asha	25	F	15days	-		L	4*5	Firm	-	-	SN	CG	HT	AG	
43	15666	esakkiyamm	42	F	5mon	-		L	5*4	Firm	-	-	SN	NCG	NTT	AG	
44	15707	petchiyamma	31	F	2mon	Pain		R	4*5	Firm	-	-	SN	LT	HT	Hash Thy	
45	16059	rajendran	33	M	1Y	-		R	2*3	Firm	-	-	SN	PC	TT	PC	
46	16063	sivaraman	35	M	3y	-		R	6*5	Firm	-	-	SN	CG	HT	FA	
47	16379	shanmugatha	55	F	2y	-		L	4*3	Firm	-	-	SN	FN	TT	FC	
48	17497	Vijaya	45	F	4mon	-		L	3*4	Firm	-	-	SN	CG	HT	FA	
49	18177	Manjula	50	F	1y	-		R	2*2	Firm	-	-	MN	AG	STT	MNG	
50	18409	Prema	43	F	1.5y	-		R	4*4	Cystic	-	-	SN	CG	HT	AG	

KEY TO MASTER CHART

AG	Adenomatous goiter
B	Benign
CA	Carcinoma
CG	Colloid goiter
FA	Follicular adenoma
FC	Follicular carcinoma
FN	Follicular neoplasm
HT	Hemithyroidectomy
L	Left
MNG	Multinodular goiter
NCG	Nodular colloid goitre
NTT	Near total thyroidectomy
PC	Papillary carcinoma
R	Right
SC	Simple cyst of thyroid
SNT	Solitary nodule thyroid
STT	Sub total thyroidectomy
TT	Total thyroidectomy